The Journal of
Thoracic Surgery

VOL. 19 MAY, 1950 NO. 5

Original Communications

PULMONARY RESECTION FOR METASTATIC MALIGNANT LESIONS

HAWLEY H. SEILER, M.D.,* O. THERON CLAGETT, M.D.,† AND
JOHN R. MCDONALD, M.D.‡
ROCHESTER, MINN.

IT IS not surprising that with the increased incidence, in recent years, of pulmonary resection for bronchiogenic carcinoma, attention should sooner or later be directed toward surgical excision of metastatic lesions. Recently Alexander and Haight[1] and Effler and Blades[2] have reported series of pulmonary resections for solitary metastatic lesions and included reviews of the literature. Prior to these reviews, only a few isolated case reports had appeared in the literature. About two years ago, a study of this subject was started at the Mayo Clinic.[3] This study included a review of the literature dealing with pulmonary metastatic phenomena and with resection for pulmonary metastatic lesions, together with a review of 10 cases in which resection had been performed at the clinic since 1941. The object of this study was to review the results obtained in all reported cases, including our own, in an effort to evaluate the worth of this procedure and to determine its place in modern thoracic surgery. Data on a total of 62 cases were assembled, including the 10 Mayo Clinic cases.

REVIEW OF THE LITERATURE

It is indeed surprising how far back attempts at surgical removal of pulmonary tissue for secondary malignant lesions can be traced. In 1898, there appeared in the German literature, an extremely interesting paper by Gerulanos,[4] in which he reported removing a portion of lung of a 15-year-old boy for a small round-cell sarcoma which had invaded from the chest wall. The patient died. Gerulanos further reviewed the data on 38 previously reported cases of chest wall tumors which had been subjected to surgical attack, and in 5 instances

Read at the Twenty-ninth Annual Meeting of The American Association for Thoracic Surgery, New Orleans, La., March 29-31, 1949.

Abridgment of thesis submitted by Dr. Seiler to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

*Fellow in Surgery, Mayo Foundation.

†Division of Surgery.

‡Division of Surgical Pathology, Mayo Clinic.

portions of lung were also removed for secondary malignant lesions. In 4 of these 5 cases the patients survived operation; 3 were reported as cured and 1 died of recurrence of sarcoma. The earliest of these 5 case reports was published in 1855 and the surgeon was a Frenchman by the name of Sedillot.[5] Of course, these early cases all represented direct spread of cancer from the chest wall rather than discrete metastatic growths.

In 1923, Meyer[6] reported the case of a left pneumonectomy performed on a boy, aged 5 years, the patient dying ten hours postoperatively. Microscopically, the lung showed lymphosarcoma and bronchiectasis. Whether or not this lesion was primary or secondary in the lung we do not know inasmuch as only partial necropsy was performed.

Perhaps the first proved and complete case history of pulmonary resection for a metastatic malignant lesion was that of Diviš[7] reported in 1927. The patient was a 42-year-old woman who had undergone ten operations in the previous thirty-five years for the removal of a recurring, slowly growing sarcoma of the left breast. A solitary tumor developed in the lower lobe of the right lung, and this was removed surgically and shown to be identical microscopically to the sarcoma of the breast. It is interesting to note that the author believed, before operation, that this lesion was metastatic, and based his decision to operate on the fact that the primary tumor was apparently a slowly growing one; the metastatic lesion appeared to be small, well defined, and solitary, and the patient was in excellent general health. At the time of the report, the patient had been well for six months with no evidence of recurrence.

Torek[8] reported an interesting case in 1930. His patient was a 42-year-old woman from whom he removed a metastatic adeno-acanthoma of the lung three years after hysterectomy for the primary tumor. The correct diagnosis was made only subsequent to operation by the pathologist. However, in commenting upon this case, Torek stated that having had such an experience, he would not be too dogmatic in refusing to remove such a metastatic lesion in the future. The patient was relieved of symptoms and was well at the time of the report.

In 1933, Lilienthal[9] reported the case of a pneumonectomy performed for a tumor of the left lung in a tuberculous patient, which proved to be metastatic from sarcoma of the uterus. The patient died on the fourth postoperative day and the primary lesion was discovered at necropsy.

Röpke[10] reported 2 cases of lobectomy for metastatic carcinoma in 1937. The primary cancers in these 2 instances were carcinoma of the breast and carcinoma of the ovary, respectively. The first patient died several months later with cerebral metastasis while the second was alive and well three and one-half years later.

In 1939, appeared the outstanding report of Barney and Churchill.[11] Their patient had been subjected to nephrectomy for adenocarcinoma in April, 1932, and pulmonary resection was performed in July, 1933, to remove a metastatic tumor. Actually, the metastatic lesion had been seen roentgenographically some time before discovery and removal of the renal tumor. This

patient was subsequently reported as being alive and well twelve years after the pulmonary operation.[12]

Experience with this case and with subsequent ones led Churchill[13] to comment, in 1940, as follows: "The status of pulmonary resection for known metastatic tumors of the lung is admittedly one of experimentation. In general, it may be taken under consideration when a solitary metastasis of a tumor of relatively low-grade malignancy appears in the lung after complete eradication of the primary growth. It is also to be considered in cases of hypernephroma with a solitary pulmonary metastasis."

In discussing all pulmonary resections for malignant disease done by him in the ten-year period prior to 1940, Churchill mentioned 5 more resections for metastatic tumors in addition to the case previously reported with Barney.

Following these early cases, each successive year has seen the appearance in the literature of additional reports of pulmonary resection for metastatic malignant tumors. In 1941, Cotton[14] mentioned a case of pneumonectomy performed for adenocarcinoma metastatic from the cecum, and Raine[15] reported a case of pneumonectomy for metastatic carcinoma originating in the sigmoid. In 1942, Freedlander and Greenfield[16] reported 2 cases, and the following year saw reports of 1 case each by King and Castleman[17] and by Brezina and Lindskog.[18] The primary sites of these 4 tumors were ovary, thyroid, stomach, and uterus. Deming and Lindskog[19] described, in 1944, a case of pneumonectomy for carcinoma metastatic from the bladder and urethra, and in the same year Blalock[20] mentioned having done a pneumonectomy for a metastatic lesion from a primary carcinoma of the rectum. In 1945, Tinney and McDonald[21] referred to a case of pneumonectomy performed at the Mayo Clinic for metastatic hypernephroma. This case is included among the report of 10 cases to be presented later in this paper.

The late Tudor Edwards,[22] in an article appearing just before his death in which he summarized his experience over the years with bronchiogenic carcinoma, made reference to the problem of pulmonary resection in secondary malignant disease. He had performed resection in 4 such cases, and 1 of the patients was alive eighteen years later. This is apparently the longest recorded survival following resection of a pulmonary metastatic lesion. Subtotal lobectomy was performed in this case, and the primary tumor was a sarcoma of the fibula. Unfortunately, no further details of the case were given. Mandeville[23] reviewed this subject and added 4 cases of his own, and Aub and Mallory added another case of lobectomy for metastatic hypernephroma (Cabot case 33,012).[24] Overholt and Langer,[25] in their paper dealing with the technique of pulmonary segmental resection, referred to 1 case of resection performed for metastatic myxosarcoma. Maier and Taylor[26] described a case of metastatic chorionepithelioma treated by lobectomy, and Rienhoff,[27] in discussing the present status of the surgical treatment of carcinoma of the lung, made reference to 4 cases of pulmonary extirpation for metastatic malignant disease. Two of these were personal cases and 2 cases were quoted from Blalock.

In August, 1947, appeared Alexander and Haight's[1] article in which 24 cases were reported. Six of these were personal cases while data on the remaining 18 were assembled from the literature and by direct inquiry from other thoracic surgeons. Some of these cases have already been mentioned but others not previously referred to include 6 cases by Sweet,[28] and 1 each by Dolley,[29] Carr,[30] and Samson.[31] Four Mayo Clinic cases were also included by these authors.

Recently, Effler and Blades[2] wrote on this subject and reported 3 cases. They also discussed some of the cases which had been reported in the literature and described 1 by Flick[32] which had not been previously reported.

REPORT OF CASES

CASE 1.—A 39-year-old housewife came to the clinic complaining of hematuria of nine months' duration. A pyelogram on admission disclosed a right renal tumor for which nephrectomy was performed in July, 1938. The pathologic examination proved this tumor to be a grade 1 hypernephroma with involvement of the renal vein by a thrombus of tumor tissue. A course of roentgen therapy was given postoperatively, and the patient remained well for several years. In July, 1940, the patient complained of pulmonary symptoms, namely, cough, chest pain, hemoptysis, and dyspnea, and a roentgenogram of the chest revealed an infiltrating lesion involving the left hilus and upper lobe (Fig. 1). Bronchoscopy revealed a

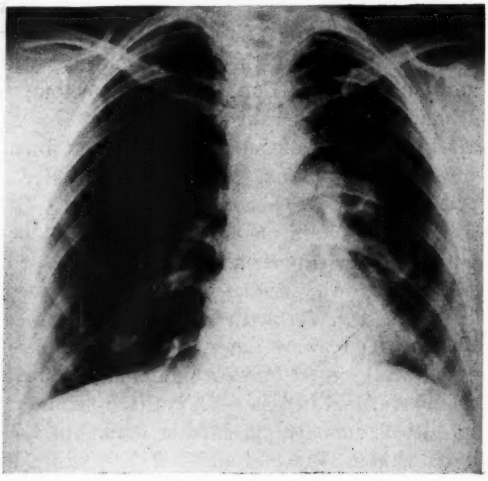


Fig. 1 (Case 1).—Infiltration of the left hilus and left upper lobe by metastatic hypernephroma.

tumor projecting into the left main bronchus, which on biopsy was reported as only inflammatory tissue. However, metastatic hypernephroma was suspected and roentgen therapy was given. In April, 1941, bronchoscopic biopsy was positive for metastatic hypernephroma, and a left pneumonectomy was performed in August, 1941.

The patient remained well for a number of years. In February, 1947, she complained of cough and occasional hemoptysis, and a roentgenogram of the chest revealed a pathologic process in the right lower pulmonary field. Symptoms progressed and in January, 1948, the patient coughed up a piece of tissue which proved histologically to be metastatic hypernephroma (Fig. 2). She finally died in May, 1948.

This patient is of interest because she survived almost seven years after pulmonary resection and because the metastatic lesion was diagnosed bronchoscopically.

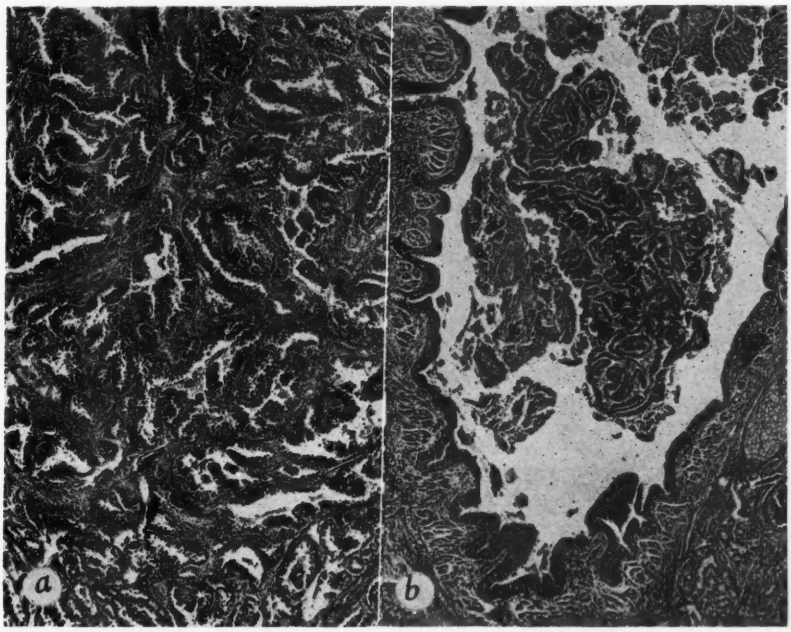


Fig. 2 (Case 1).—*a*, Primary hypernephroma of the kidney, showing characteristic grouping of neoplastic cells (hematoxylin and eosin ×25). *b*, Metastatic hypernephroma of the left lung with a pattern similar to that of the primary tumor. The section shows tumor tissue within a major bronchus (hematoxylin and eosin ×25).

CASE 2.—A 38-year-old housewife was seen in March, 1943, with two major pathologic findings: one, an obstructing, annular carcinoma of the rectum, and the other, roentgenographic evidence of a mass in the lower portion of the right hilar region. Biopsy of both lesions showed them to be identical grade 1 adenocarcinomas. A preliminary colostomy was done, and during the interval before proceeding with resection of the bowel, a right pneumonectomy was performed. This was followed in several months by anterior resection of the pelvic colon with end-to-end anastomosis. The patient remained well for about one and one-half years at which time she returned with obstruction of the bowel and abdominal carcinomatosis. She died two months later.

CASE 3.—A 40-year-old white barber was seen in August, 1943, with a spherical mass in the apex of the left lung. He had complained of hemoptysis for fourteen months. Vague abdominal symptoms in the form of dyspepsia and loose stools were occasionally noted also. Pneumonectomy was performed, and the specimen histologically proved to be an anaplastic, grade 4 carcinoma showing feeble attempts at gland formation. On the twenty-first postoperative day, abdominal pain and rigidity developed, and evidence of a perforated viscus and peritonitis soon became evident. General toxicity and shock rapidly developed and in forty-eight hours the patient was dead. Post-mortem examination revealed a tumor of the jejunum which had perforated with resulting peritonitis and death. Microscopically, the tumor closely resembled the lesion in the lung and was thought to be the primary tumor in this case, with the pulmonary lesion being a metastatic one.

Fig. 3 (Case 5).—Metastatic lesion in the right upper lobe close to the mediastinum.

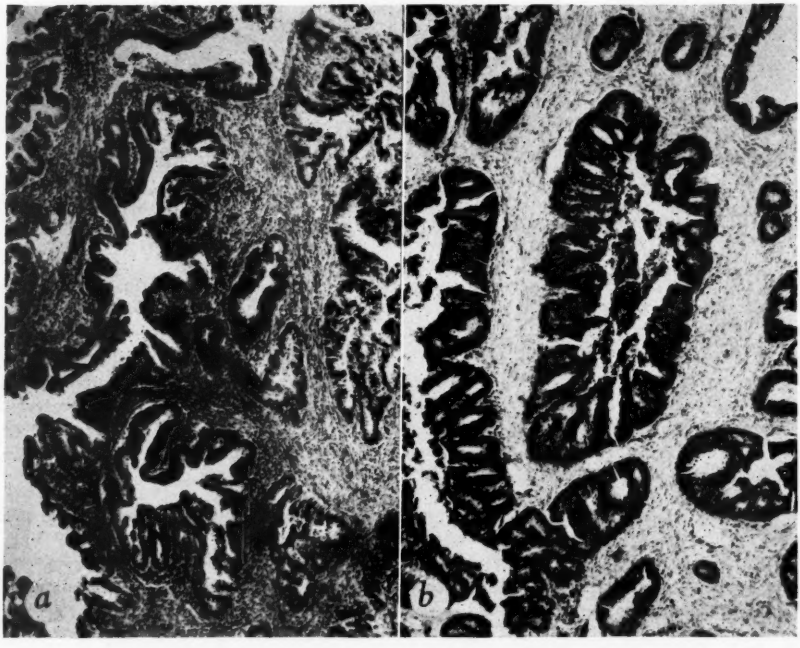


Fig. 4 (Case 5).—*a*, Primary grade 2 adenocarcinoma of the rectum with papillary infoldings (hematoxylin and eosin ×55). *b*, Metastatic grade 2 adenocarcinoma of the lung; similar in pattern to primary rectal tumor (hematoxylin and eosin ×55).

This case is a good example of what Willis[33] referred to as a "latent primary neoplasm" in which the first indication of cancer is manifest by the appearance of a "precocious metastasis."

CASE 4.—A 25-year-old physician was seen in May, 1944, fourteen months subsequent to left orchidectomy for teratoma. There were no pulmonary symptoms, but a roentgenogram of the chest revealed a lobulated shadow in the lower right pulmonary field. The lesion failed to respond to irradiation therapy, and consequently a right lower lobectomy was performed. As suspected, the extirpated portion of lung contained metastatic teratoma. This patient survived twenty-one months following pulmonary resection and died as the result of further intrapulmonary metastasis.

CASE 5.—In August, 1941, a 46-year-old man was subjected to posterior resection of the rectum following preliminary loop colostomy for grade 2, ulcerating adenocarcinoma. The patient remained well for four years. At the time of the periodic re-examination in October, 1945, a solitary nodule in the right upper lobe was seen on the roentgenogram (Fig. 3). There were no symptoms. Right upper lobectomy was performed in November, 1945, and the excised lesion presented a histologic pattern identical to that of the previously removed rectal carcinoma (Fig. 4). Unfortunately, cerebral metastatic lesions developed eight months later, and the patient died about a year after lobectomy.

CASE 6.—A 34-year-old man underwent amputation of the right leg in January, 1942, for a recurrent, grade 1 chondrosarcoma with areas of osteogenic sarcoma of the os calcis. The tumor had been locally excised on four previous occasions. After amputation he remained well for about four years, and then returned to the clinic complaining of productive cough, dyspnea, and a recent acute respiratory infection. A roentgenogram revealed a mass in the right upper pulmonary field that contained areas of calcification. Pulmonary resection was advised and a right upper lobectomy performed. It was impossible to remove all of the tumor at the time of operation, however, owing to mediastinal and chest wall involvement, so that the procedure must be classed as a frankly palliative one. Pathologic examination showed this tumor to be an osteogenic sarcoma also. The patient survived only several months after operation.

CASE 7.—A 23-year-old housewife was first seen at the clinic in 1924, at which time electrosurgical excision of an adenocarcinoma, mixed tumor type, of the alveolar process was done. The tumor recurred locally in 1927, and was again removed by destroying the entire site with diathermy. Postoperative radium therapy was used each time.

The patient remained well for many years and returned in April, 1946, at which time a well-circumscribed, nodular tumor was found in the right midpulmonary field (Fig. 5). Pneumonectomy was performed and the extirpated lesion was demonstrated to be a metastatic adenocarcinoma, mixed tumor type (Fig. 6). Some months later the patient returned with further peripheral metastatic growths in the right breast, the scalp, and the left groin. These were proved by biopsy. She died one year after pulmonary resection owing to further metastatic spread, principally intra-abdominal.

CASE 8.—A 28-year-old farmer was seen at the clinic in October, 1946, with a pulmonary tumor obstructing the bronchi of the right middle and lower lobes and producing partial atelectasis. History disclosed orchidectomy three years before for a grade 4 malignant tumor. Biopsy of the lesion in the lung showed it to be a grade 4 squamous cell epithelioma. A right pneumonectomy was performed with uneventful recovery. Histologic comparison of the two tumors showed them to be similar, both lesions proving to be grade 4 mixed squamous-cell epithelioma and adenocarcinoma. A two months' follow-up indicated recurrence of the pulmonary lesion, and the patient lived only four months after resection.

CASE 9.—A 20-year-old girl presented two lesions: a recurrent fibrosarcoma of the lower part of the right leg, and a well-circumscribed roentgenographic shadow in the right lower

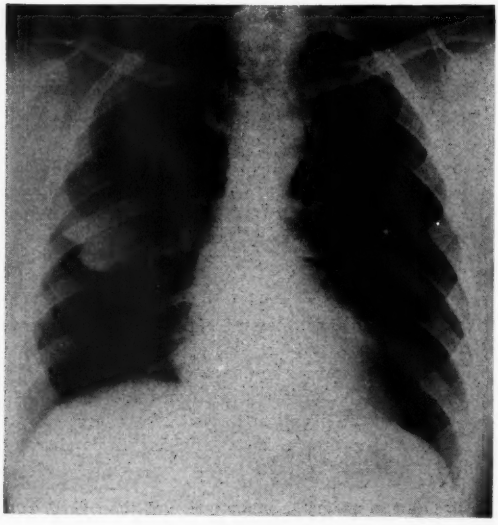


Fig. 5 (Case 7).—Nodular, metastatic tumor in the right lung.

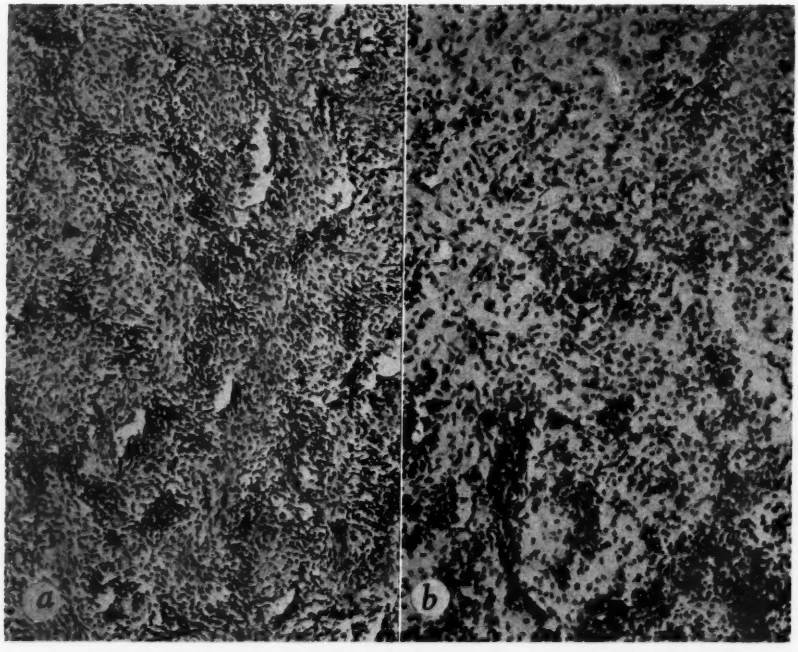


Fig. 6 (Case 7).—*a*, Primary adenocarcinoma of the jaw, mixed tumor type. Cartilage formation can be seen (hematoxylin and eosin ×85). *b*, Metastatic adenocarcinoma of the lung, mixed tumor type, with epithelial cords between areas of cartilage (hematoxylin and eosin ×85).

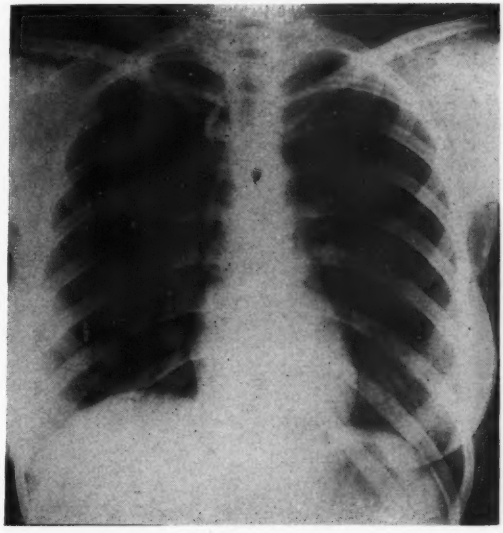


Fig. 7 (Case 9).—Well-circumscribed, metastatic fibrosarcoma peripherally situated in the right lower pulmonary field.

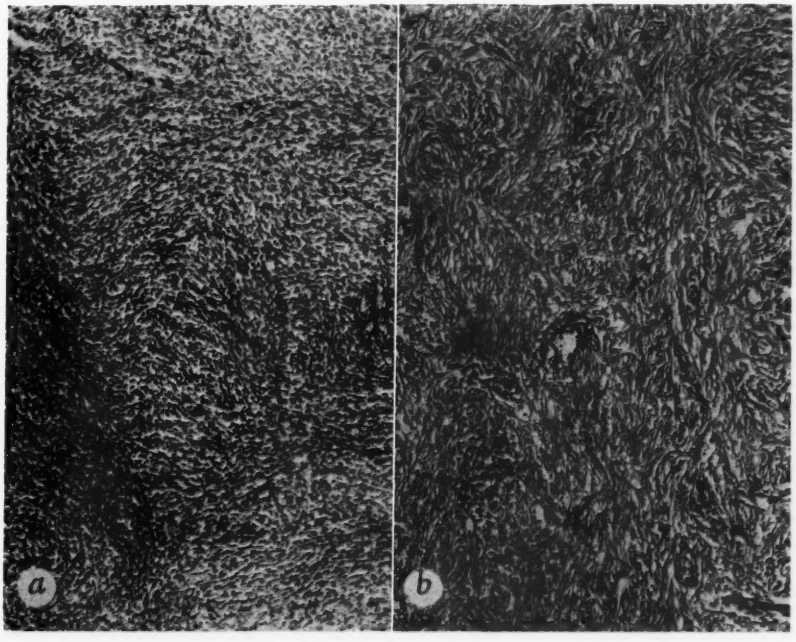


Fig. 8 (Case 9).—*a*, Primary grade 1 fibrosarcoma of the right leg; spindle-shaped cells are compactly arranged (hematoxylin and eosin ×85). *b*, Metas atic grade 1 fibrosarcoma of the lung; the pattern of interlacing bundles is similar to that in *a* (hematoxylin and eosin ×85).

pulmonary field (Fig. 7). The tumor of the leg had been removed in 1935, and again in 1939, and review of the histologic sections showed it to be a slowly growing, grade 1 fibrosarcoma. The patient steadfastly refused amputation. In October, 1946, right lower lobectomy was per-

Fig. 9 (Case 10).—Metastatic tumor in the right lower pulmonary field.

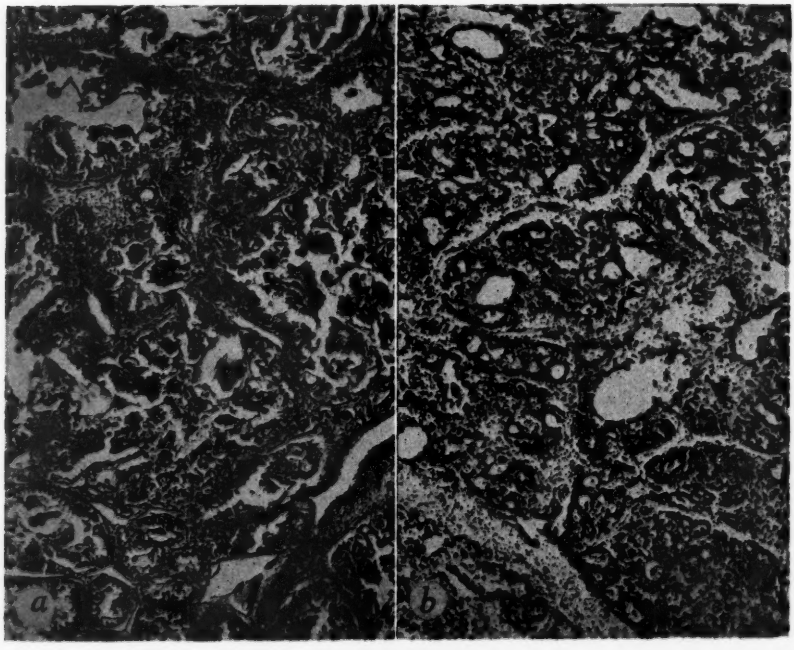


Fig. 10 (Case 10).—*a*, Primary ovarian tumor, a grade 4, papillary colloid adenocarcinoma (hematoxylin and eosin ×50). *b*, Metastatic tumor of the lung showing similar grade 4, papillary, colloid adenocarcinoma (hematoxylin and eosin ×55).

formed, and the tumor of the leg was again widely excised. Pathologic examination of the two lesions showed them to be identical in every respect (Fig. 8). The patient has been heard from a number of times and has remained well.

CASE 10.—A 51-year-old housewife was seen in January, 1947, when a well-circumscribed tumor was visible roentgenographically in the base of the right lung (Fig. 9). She had had two previous operations for cancer, the first being enucleation of the right eye in 1936, because of melano-epithelioma, and the second being right oophorectomy and hysterectomy in 1943, for adenocarcinoma of the ovary. Bronchoscopic biopsy of the pulmonary tumor showed it to be adenocarcinoma, and a right lower lobectomy was performed. Histologic comparison of the removed pulmonary tumor and the original carcinoma of the ovary showed them both to be grade 4, papillary adenocarcinoma (Fig. 10). This patient has remained well with no evidence of recurrence.

ANALYSIS OF DATA ON MAYO CLINIC CASES

Type of Primary Tumor.—Of the 10 cases reported herein, 5 represented carcinomas, 3 mixed tumors, and 2 sarcomas. The mixed tumors were predominantly carcinomatous, however, and have been included as such in Table I.

TABLE I. TYPE OF PRIMARY TUMOR (MAYO CLINIC CASES) FOR WHICH PULMONARY RESECTION OF THE METASTATIC LESION WAS CARRIED OUT

TYPE OF PRIMARY TUMOR	CASES	
Carcinoma		8
Mixed tumor (adenocarcinoma of jaw, mixed tumor type, 1; mixed squamous-cell epithelioma and adenocarcinoma of testis, 1; teratoma of testis, 1)	3	
Adenocarcinoma of rectum	2	
Adenocarcinoma of jejunum	1	
Adenocarcinoma of ovary	1	
Hypernephroma	1	
Sarcoma		2
Osteogenic sarcoma of os calcis	1	
Fibrosarcoma of leg	1	

Symptoms.—A review of the symptoms elicited from the various patients at the time of discovery of the pulmonary lesion is of relatively little value as an aid to diagnosis. Three patients were asymptomatic. Cough and dyspnea were the two most common symptoms, each being complained of by 4 patients. In 3 patients hemoptysis had been experienced, and 3 patients complained

TABLE II. SURVIVAL PERIOD FOLLOWING PULMONARY RESECTION FOR A METASTATIC MALIGNANT LESION (MAYO CLINIC CASES)

CASE	SURVIVAL (MONTHS)	PRESENT STATUS OF PATIENT
1	81	Dead
2	24	Dead
3	23 days	Dead
4	21	Dead
5	12	Dead
6	3	Dead
7	12	Dead
8	4	Dead
9	28	Alive and well
10	24	Alive and well

TABLE III. PULMONARY RESECTION FOR METASTATIC MALIGNANT LESIONS: DATA ON SIXTY-TWO REPORTED CASES INCLUDING TEN MAYO CLINIC CASES

REPORT			TIME INTERVAL (MONTHS)				MONTHS AFTER PULMONARY RESECTION		
YEAR	AUTHOR	PRIMARY LESION	PRIMARY TUMOR TO METASTASIS	REMOVAL OF PRIMARY TUMOR TO PULMONARY RESECTION	OPERATION	BRONCHIAL INVOLVEMENT	WITHOUT RECURRENCE	UNTIL RECURRENCE	UNTIL DEATH
1927	Diviš[7]	Sarcoma, breast	(a)	(a)	Remove metastasis	No data	6	(b)	
1930	Torek[8]	Adeno-acanthoma, uterus	24	36	Remove metastasis	No data	No data		
1933	Lilienthal[9]	Sarcoma, uterus	(c)	(c)	Pneumonectomy	No			4 days
1937	Röpke[10] (Case 1)	Carcinoma, breast	36	36	Lobectomy	No data		(d)	4½
1937	Röpke (Case 2)	Carcinoma, ovary	29	36	Lobectomy	No data	42		
1939	Barney and Churchill[11] (Case 1)	Renal adenocarcinoma	(e)	15	Partial lobectomy	No data	144		Well
1940	Churchill[13] (Case 2)	Not stated			Partial lobectomy	No data	No data	No data	
1940	Churchill (Case 3)	Not stated			Bilateral partial lobectomy (2 operations)	No data	No data	No data	
1940	Churchill (Case 4)	Not stated			Lobectomy	No data	No data	No data	
1940	Churchill (Case 5)	Not stated			Lobectomy	No data	No data	No data	
1940	Churchill (Case 6)	Not stated			Pneumonectomy	No data	No data	No data	
1941	Cotton[14]	Adenocarcinoma, cecum	48	48	Pneumonectomy	Yes	36		
1941	Raine[15]	Carcinoma, sigmoid	9	21	Pneumonectomy	Yes		3	
1942	Freedlander and Greenfield[16] (Case 1)	Granulosa-cell tumor, ovary	(f)	(g)	Pneumonectomy	Yes	6		
1942	Freedlander and Greenfield (Case 2)	Adenocarcinoma, thyroid	480	480	Pneumonectomy	Yes			1 day
1943	King and Castleman[17]	Carcinoma, stomach	(c)	(c)	Lobectomy	Yes			2 days
1943	Brezina and Lindskog[18]	Carcinoma, uterus	156	162	Pneumonectomy	Yes		17	24
1944	Deming and Lindskog[19]	Carcinoma, bladder and urethra	144 to 9 (h)	150 to 15 (h)	Pneumonectomy	No		2	5½
1944	Blalock[20] (Case 1)	Carcinoma, rectum	43	54	Pneumonectomy	No data	37		
1945	Tinney and McDonald[21] (Mayo Clinic, Case 1)	Hypernephroma	24	37	Pneumonectomy	Yes		66	81
1946	Edwards[22] (Case 1)	Squamous-cell epithelioma, palate	Not stated		Lobectomy	No data	No data	No data	15
1946	Edwards (Case 2)	Carcinoma, rectum	Not stated		Pneumonectomy	No data	No data	No data	15
1946	Edwards (Case 3)	Carcinoma, rectum	Not stated		Wedge resection	No data	No data (i)	No data (i)	

1946	Edwards (Case 4)	Sarcoma, fibula	Not stated		Subtotal lobectomy	No data	216		Well
1946	Mandeville[23] (Case 1)	Fibrosarcoma, arm	60 to 12 (j)	60 to 12 (j)	Pneumonectomy	No data			Death at operation
1946	Mandeville (Case 2)	Granulosa-cell tumor, ovary	72	72	Pneumonectomy	No data		8½ (?)	8½
1946	Mandeville (Case 3)	Malignant melanoma	48	48	Pneumonectomy	No data		12 (?)	12
1946	Mandeville (Case 4)	Carcinoma, cervix	36	36	Pneumonectomy	No data	(k)	(k)	
1947	Aub and Mallory (Cabot case 33,012)[24]	Hypernephroma	72	72	Lobectomy	Yes		"Several"	Several
1947	Overholt and Langer[25]	Myxosarcoma, site?	Not stated		Segmental resection	No data	No data	No data	
1947	Maier and Taylor[26]	Chorionepithelioma	36	48	Lobectomy	No	36		Well
1947	Rienhoff[27] (Case 1)	Fibrosarcoma, tendon sheath	Not stated		No data	No data	No data	No data	
1947	Rienhoff (Case 2)	Fibrosarcoma, tendon sheath	Not stated		No data	No data	No data	No data	
1947	Alexander and Haight[1] (Case 1)	Neurogenic sarcoma, ulnar nerve	18	25¾ to 13 (l)	Bilateral lobectomy	No	74	7	
1947	Alexander and Haight (Case 2)	Myogenic sarcoma, thigh	19	21	Lobectomy	No	48		
1947	Alexander and Haight (Case 3)	Fibrosarcoma, thigh	24	29	Double lobectomy	Yes	13		
1947	Alexander and Haight (Case 4)	Carcinoma, rectum	48	72	Pneumonectomy	Yes		3	5
1947	Alexander and Haight (Case 5)	Spindle-cell sarcoma, leg	4	5	Pneumonectomy	No		1¾	Impending
1947	Alexander and Haight (Case 6)	Renal cell carcinoma	61	66¾	Pneumonectomy	Yes	1	(m)	(m)
1947	Sweet[28] (Case 1)	Sarcoma, breast	48	48	Pneumonectomy	No data	84		
1947	Sweet (Case 2)	Carcinoma, ovary	120	120	Lobectomy	No data		12	12 plus
1947	Sweet (Case 3)	Fibrosarcoma, chest wall	26	26	Lobectomy	No data	9		
1947	Sweet (Case 4)	Renal cell carcinoma	¾	¾	Lobectomy	No data	15		
1947	Sweet (Case 5)	Renal cell carcinoma	2	2	Lobectomy	No data		1½	Unknown
1947	Sweet (Case 6)	Renal cell carcinoma	24	24	Partial lobectomy	No data		9	
1947	Dolley[29]	Carcinoma, mandible	108	112	Lobectomy	No data			3 days
1947	Carr[30]	Osteogenic sarcoma, thigh	49	58	Pneumonectomy	No data		5 plus	10
1947	Samson[31]	Carcinoma, colon	72	73½	Lobectomy	No	3½		
1948	Effler and Blades[2] (Case 1)	Malignant synovioma, calf	24	2	Lobectomy	No data	17		
1948	Effler and Blades (Case 2)	Carcinoma, sigmoid	14	22	Lobectomy	No data	18 (n)	(n)	
1948	Effler and Blades (Case 3)	Teratocarcinoma, testis	10	17	Lobectomy	No data		4	

(*Continued on following page.*)

TABLE III—CONCLUDED

REPORT			TIME INTERVAL (MONTHS)				MONTHS AFTER PULMONARY RESECTION		
YEAR	AUTHOR	PRIMARY LESION	PRIMARY TUMOR TO METASTASIS	REMOVAL OF PRIMARY TUMOR TO PULMONARY RESECTION	OPERATION	BRONCHIAL INVOLVEMENT	WITHOUT RECURRENCE	UNTIL RECURRENCE	UNTIL DEATH
1948	Blalock[34] (Case 2)	Adenocarcinoma, cecum	39	48	Pneumonectomy	No data	5		
1948	Flick[32]	Liposarcoma, thigh	96	96	Lobectomy	No data	16		
1948	Mayo Clinic (Case 2)	Adenocarcinoma, rectum	(f)	(g)	Pneumonectomy	Yes		20	24
1948	Mayo Clinic (Case 3)	Adenocarcinoma, jejunum	(e)	(g)	Pneumonectomy	No			23 days (p)
1948	Mayo Clinic (Case 4)	Teratoma, testis	11	15	Lobectomy	No		18	21
1948	Mayo Clinic (Case 5)	Adenocarcinoma, rectum	50	51	Lobectomy	Yes		8	12
1948	Mayo Clinic (Case 6)	Osteogenic sarcoma, os calcis	(q)	(q)	Lobectomy	Yes		3(q)	3 plus
1948	Mayo Clinic (Case 7)	Adenocarcinoma of jaw, mixed tumor type	(r)	270 to 234	Pneumonectomy	Yes		5	12
1948	Mayo Clinic (Case 8)	Mixed squamous-cell and adenocarcinoma, testis	36	36	Pneumonectomy	Yes		2	4
1948	Mayo Clinic (Case 9)	Fibrosarcoma, leg	(s)	132 to 84 (s)	Lobectomy	No	28		Well
1948	Mayo Clinic (Case 10)	Adenocarcinoma, ovary	42	48	Lobectomy	Yes	24		Well

(a) Ten operations over a 34-year period (from the age of 7 to 41 years) for removal of recurring sarcoma of breast. First removal, 35 years previously; last removal, 1 year previously.
(b) Followed up 6 months.
(c) Metastatic lesion removed first; necropsy revealed primary growth.
(d) Cerebral metastasis occurred after several months.
(e) Metastatic lesion discovered first.
(f) Primary and secondary lesions discovered simultaneously.
(g) Metastatic tumor removed first.
(h) Multiple operations for recurring carcinoma of bladder and urethra over a 12-year period.
(i) Untraced after 6 months.
(j) During the 5-year period prior to pneumonectomy, 4 local excisions of the primary tumor had been done, culminating in amputation 1 year prior to pulmonary resection.
(k) Too recent to evaluate. Patient still living but hilar nodes involved.
(l) Two operations on metastatic lesions 13 months apart.
(m) Interval not sufficient to permit evaluation; prognosis seems poor.
(n) An intracranial metastatic lesion was removed by craniotomy 5 months after pulmonary resection; patient well 1½ years after lobectomy.
(p) Death due to rupture of previously silent carcinoma of the jejunum, the primary lesion, found at necropsy.
(q) First amputation of leg 4½ years previously; second amputation 4 years previously; lobectomy was frankly palliative.
(r) First operation on primary lesion 22 years before; second operation on primary lesion 19 years before.
(s) Two previous operations on primary tumor 11 and 7 years before, respectively; third operation for removal of primary growth performed at time of pulmonary resection.

of pain in the chest. In 3 other patients the only finding was a positive result on roentgenologic examination of the chest. Two patients complained of a recent acute respiratory infection and 2 of wheezing.

Time Interval Between Removal of the Primary Tumor and the Appearance of the Metastatic Pulmonary Lesion.—This interval of time varied from eleven months to twenty-two years. In 2 cases, the metastatic growth was removed first. In 3 instances there were multiple excisions of the primary tumor before the appearance of the metastatic lesion.

Bronchial Involvement.—Gross bronchial involvement was demonstrated in 7, or 70 per cent, of the 10 cases. In 4 of the 10 cases, positive tissue evidence of malignancy was obtained by means of bronchoscopic biopsy.

Survival Periods.—Of the 10 patients, 8 are now dead and 2 are living and well with no evidence of recurrence. The longest survival following pulmonary resection for a metastatic lesion in this group was six years and nine months (Table II).

ANALYSIS OF DATA ON ALL SIXTY-TWO REPORTED CASES

This group includes the 52 cases reported in the literature plus the 10 Mayo Clinic cases reported herein. The pertinent data relative to these 62 cases have been arranged in tabular form and are listed by year of publication and author (Table III).

Type of Primary Tumor.—In 57 instances the type of the primary tumor was mentioned by the author. Of these, 18 were sarcomas, 35 were carcinomas, and 4 were of the mixed tumor type. Of the 4 mixed tumors, 1 was a mixed tumor of the jaw, 1 was a mixed squamous-cell epithelioma and adenocarcinoma of the testis, and 2 were teratoma of the testis. Inasmuch as the carcinomatous element predominated in all of these tumors, they have been classified among the carcinomas for the sake of simplicity (Table IV). A review of this information indicates that the most common primary site in the entire series was carcinoma of the large bowel (11 cases); of these, 6 were rectal carcinomas. The primary tumor was hypernephroma in 7 instances and fibrosarcoma in 7 instances. Carcinoma of the ovary was fourth in frequency, with the lesion in 5 cases being primary in this organ.

Time Interval Between Removal of the Primary Tumor and the Appearance of the Metastatic Pulmonary Lesion.—This, of course, was extremely variable ranging from zero to forty years (Freedlander and Greenfield's Case 2).[16] In several instances the metastatic lesion was discovered prior to the primary growth or simultaneously. Although the primary carcinoma of the thyroid was removed forty years before in the case referred to previously, a small local recurrence of the tumor in the thyroid gland was found at necropsy. In Diviš'[17] case, the patient had undergone ten local removals of a sarcoma of the breast over a period of thirty-five years before the occurrence of the pulmonary lesion. Deming and Lindskog's[19] patient also had multiple removals of the primary neoplasm of the bladder and urethra over a twelve-year period. Thus, the true time interval before pulmonary metastasis occurred cannot be accurately estimated in these cases. In 7 instances, the interval of time elapsing

(r) First operations on primary tumor 11 and 7 years before, respectively; third operation for removal of primary growth performed at time of pulmonary resection.
(s) Two previous operations for removal of primary tumor.

TABLE IV. TYPES OF PRIMARY TUMORS FOR WHICH PULMONARY RESECTION OF THE METASTATIC LESION WAS CARRIED OUT (ALL REPORTED CASES)

TYPE OF PRIMARY TUMOR	CASES	
Carcinoma (68 per cent)		39
Adenocarcinoma of large bowel (cecum 2, sigmoid 2, colon 1, rectum 6)	11	
Hypernephroma	7	
Carcinoma of ovary (adenocarcinoma 3, granulosa-cell carcinoma 2)	5	
Carcinoma of uterus (adeno-acanthoma 1, adenocarcinoma 1)	2	
Mixed tumor type (teratoma of testis 2, squamous-cell epithelioma and adenocarcinoma of testis 1, mixed tumor of jaw 1)	4	
Carcinoma of cervix	1	
Chorionepithelioma	1	
Carcinoma of breast	1	
Carcinoma of thyroid	1	
Carcinoma of stomach	1	
Adenocarcinoma of jejunum	1	
Carcinoma of bladder and urethra	1	
Squamous-cell epithelioma of palate	1	
Carcinoma of mandible (adamantinoma)	1	
Malignant melanoma	1	
Sarcoma (32 per cent)		18
Fibrosarcoma (tendon sheath 2, leg 2, thigh 1, arm 1, chest wall 1)	7	
Osteogenic sarcoma (thigh 1, os calcis 1)	2	
"Sarcoma" (breast 2, uterus 1, fibula 1)	4	
Myxosarcoma	1	
Neurogenic sarcoma	1	
Myogenic sarcoma	1	
Liposarcoma	1	
Malignant synovioma of calf	1	

between removal of the primary tumor and the appearance of the metastatic lesion in the lung was, or could have been, ten years or longer (Table V). The usual time interval was much less than the extremes indicated in Table V, however, averaging one to four years. In some instances the metastatic growth was evident in a matter of only a few months. In the group of 7 "long interval" cases, 5 patients died, 1 was alive two years after pulmonary resection, and the remaining 1 was followed only six months.

Bronchial Involvement.—In 27 of the 62 cases, a definite statement was given concerning the presence or absence of involvement of a major bronchus

TABLE V. TIME INTERVAL BETWEEN REMOVAL OF PRIMARY TUMOR AND APPEARANCE OF PULMONARY METASTATIC LESION IN SEVEN CASES IN WHICH DURATION WAS LONGEST

AUTHOR	INTERVAL (YEARS)
Freedlander and Greenfield[16], Case 2	0 to 40
Diviš*[7]	1 to 35
Mayo Clinic, Case 7*	19 to 22
Brezina and Lindskog[18]	13
Deming and Lindskog*[19]	1 to 12
Mayo Clinic, Case 9*	7 to 11
Sweet,[2] Case 2	10

*Multiple operations performed for recurring primary tumor.

or branch by the metastatic tumor. In 17 cases (63 per cent), bronchial involvement was present and in 10 cases it was not. By inference it may be assumed that in most of the remaining cases in which this feature was not discussed, gross bronchial involvement was probably not present. For the entire series of 62 cases, the incidence of bronchial involvement as definitely stated was 27 per cent (17 out of 62 cases). The true percentage undoubtedly lies somewhere between this figure and the previously mentioned 63 per cent, probably 35 to 40 per cent of cases.

Of the 17 cases in which bronchial involvement was noted in this series, there was a positive result on bronchoscopic biopsy in 10 (59 per cent). This is an incidence of 16 per cent for positive results on biopsy for the entire series.

Type of Operation Performed.—Of the 62 patients reported on, 27 had lobectomy, 25 had pneumonectomy, and 10 had partial lobectomy or segmental resection. Two patients had multiple removal of pulmonary metastatic tumors, of which 1 was by lobectomy on two separate occasions, and 1 by bilateral partial lobectomy. Two instances listed as segmental resection were probably simple excision of the metastatic nodule. In the cases reported early, partial lobectomy and local excision were not infrequently performed, whereas pneumonectomy was usually the procedure of choice in the cases in which operation was performed during the middle years. More recently, lobectomy has been done more often than any other procedure, and superficially it appears that the best results have been obtained from this procedure (Table VI). It is impossible to convey accurately the entire picture by this means, however, inasmuch as the figures do not take into consideration such important factors as extent of the lesion at the time of operation, operative and postoperative mortality, and the time interval between discovery of the metastatic growth and surgical excision. It is probably true, nevertheless, that in the case of a solitary metastatic tumor well within the confines of one lobe, lobectomy is the procedure of choice. Segmental or wedge resection may occasionally be considered in selected cases.

TABLE VI. SURVIVAL ACCORDING TO TYPE OF OPERATIVE PROCEDURE CARRIED OUT

OPERATIVE PROCEDURE	PATIENTS		
	OPERATED ON	SURVIVING	
		NUMBER	PER CENT
Partial or segmental lobectomy	10	3	30
Lobectomy	27	13	48
Pneumonectomy	25	7	28

End Results.—Of the 62 patients who underwent pulmonary resection for metastatic lesions, 23 were living and well at the time of the various reports (37 per cent). This figure is obviously too high inasmuch as some of the patients had been followed for only a short time. Furthermore, some of the patients who were well at the time of reporting will likely have died subsequently of further spread of their disease. In an occasional instance, the patient was alive and well but the author commented upon the unfavorable prognosis in view of involved hilar glands at the time of operation, or other

TABLE VII. DATA ON TWENTY-THREE PATIENTS WHO UNDERWENT PULMONARY RESECTION FOR A METASTATIC MALIGNANT LESION OF THE LUNG AND WHO WERE ALIVE WHEN THE CASES WERE REPORTED

AUTHOR	SURVIVAL (MONTHS)	PRIMARY TUMOR
Diviš[7]	6	Sarcoma of breast
Röpke,[10] Case 2	42	Carcinoma of ovary
Barney and Churchill[11]	144	Hypernephroma
Cotton[14]	36	Carcinoma of cecum
Freedlander and Greenfield,[16] Case 1	6	Granulosa-cell carcinoma of ovary
Blalock,[20] Case 1	37	Carcinoma of rectum
Edwards,[22] Case 4	216	Sarcoma of fibula
Mandeville,[23] Case 4	3 (?)	Carcinoma of cervix
Maier and Taylor[26]	36	Chorionepithelioma
Alexander and Haight,[1] Case 1	74	Neurogenic sarcoma of ulnar nerve
Alexander and Haight, Case 2	48	Myogenic sarcoma of thigh
Alexander and Haight, Case 3	13	Fibrosarcoma of thigh
Alexander and Haight, Case 6	1	Hypernephroma
Sweet,[28] Case 1	84	Sarcoma of breast
Sweet, Case 3	9	Fibrosarcoma of chest wall
Sweet, Case 4	15	Hypernephroma
Samson[31]	3½	Carcinoma of colon
Effler and Blades,[2] Case 1	17	Malignant synovioma
Effler and Blades, Case 2	18	Carcinoma of sigmoid
Blalock,[34] Case 2	5	Carcinoma of cecum
Flick[32]	16	Liposarcoma of thigh
Mayo Clinic, Case 9	28	Fibrosarcoma of leg
Mayo Clinic, Case 10	24	Adenocarcinoma of ovary

modifying circumstances. In 1 instance the patient subsequently had an intracranial metastatic lesion which was removed by craniotomy (Effler and Blades,[2] Case 2). The patient was alive and well one and one-half years after lobectomy, and thirteen months after craniotomy. This is indeed carrying extirpative surgery to great lengths.

Study of the surviving 23 patients yields certain interesting information (Table VII). It appears, for instance, that Edwards'[22] patient (Case 4) has survived the longest to date, namely, eighteen years. Unfortunately, this case was not described in any detail. The next longest survival was the patient of Barney and Churchill[11] who was alive and well twelve years later. The operation in the latter case was done for metastatic hypernephroma, and in Edwards' case it was done for sarcoma of the fibula. Sweet[28] has had a seven-year survival following resection for metastatic sarcoma of the breast, and Alexander and Haight's[1] first patient was alive and well six years and two months subsequent to resection for a metastatic neurogenic sarcoma. It is noteworthy that 3 of these 4 long survivals represented cases of sarcoma and the fourth represented a hypernephroma, a tumor well known to give rise to solitary metastatic lesions of the lung. Partial lobectomy was the operative procedure carried out in Edwards'[22] case and in Barney and Churchill's[11] case, while pneumonectomy was done in Sweet's[28] case, and bilateral lobectomy was performed in the case of Alexander and Haight.[1] The last-mentioned patient had 2 metastatic growths removed thirteen months apart and was alive and well six years and two months later.

Table VIII gives the distribution of the primary lesion according to site in the 23 cases in which the patient was alive at the time of the report.

TABLE VIII. PRIMARY LESION IN TWENTY-THREE CASES IN WHICH THE PATIENT WAS ALIVE AT THE TIME THE CASE WAS REPORTED

TYPE OF TUMOR		CASES
Carcinoma		13
Large bowel (cecum 2, sigmoid 1, colon 1, rectum 1)	5	
Hypernephroma	3	
Ovary	3	
Cervix	1	
Chorionepithelioma	1	
Sarcoma		10
Fibrosarcoma (thigh, leg, chest wall)	3	
Breast	2	
Osteogenic, fibula	1	
Neurogenic, ulnar nerve	1	
Myogenic, thigh	1	
Liposarcoma, thigh	1	
Malignant synovioma	1	

In 10 instances in the group of 23 surviving patients, the presence or absence of bronchial involvement was commented upon by the author. Of this number, 5 patients showed invasion of a major bronchus by the tumor and 5 did not.

In some instances in which there was a final fatal outcome, pulmonary resection resulted in such a degree of palliation and prolongation of life as to make the procedure definitely worth while. In the Mayo Clinic Case 1, for example, the patient lived six years and nine months before eventually dying of further metastasis, and most of this time she was well. Usually the interval between pulmonary resection for a metastatic lesion and death has been of short duration. Thus, it appears that in the majority of cases, if further spread is going to occur after pulmonary resection, it will probably be apparent within a period of several months to one and one-half years or two years.

Six operative or immediate postoperative deaths occurred in the entire series of 62 cases, an incidence of 10 per cent.

SUMMARY

Reports of 52 cases in the literature plus the records of 10 cases at the Mayo Clinic in which pulmonary resection was performed for metastatic malignant lesions have been studied and the findings presented.

The primary tumor was sarcoma in 32 per cent (18 cases), and carcinoma in 68 per cent (39 cases) of the 57 cases in which the type of primary tumor was mentioned. The primary tumors for which resection of solitary pulmonary metastatic lesions was most frequently done were carcinoma of the large bowel (11 cases), hypernephroma (7 cases), fibrosarcoma (7 cases), and carcinoma of the ovary (5 cases).

The time intervals between removal of the primary tumor and appearance of the secondary lesion in the lung were extremely variable, ranging from zero to forty years. With several exceptions, the patients with long intervals of time elapsing between the occurrence of the primary and the secondary tumors did no better than the group as a whole.

Bronchial involvement was noted in 63 per cent of the cases in which the reports especially mentioned this feature, or in 27 per cent of the entire group. The true percentage probably lies somewhere between these two figures, indicating that in a very substantial proportion of cases the tumor will be found to be invading a major bronchus. This is in contradistinction to the former teaching that bronchial invasion by a metastatic tumor is uncommon. A positive diagnosis was made by means of bronchoscopic biopsy in 16 per cent of the entire series.

The type of operation performed apparently did not too greatly influence the survival rate. Lobectomy or segmental resection is probably the procedure of choice when possible.

Twenty-three patients out of 62 were living and well at the time reported on (37 per cent). Two of these 23 had survived ten years or longer, and 7 more had survived for periods ranging from three to ten years. The remaining 14 patients had been living and well for periods varying from several months to two years after resection. Of the group of 23 survivors, the primary lesion was sarcoma in 10 instances and carcinoma in 13. The most common primary tumors encountered among the surviving group were carcinoma of the colon and rectum, hypernephroma, fibrosarcoma, and carcinoma of the ovary.

Palliative pulmonary resection for metastatic malignant lesions occasionally seemed to be justifiable on the basis of prolongation of life (six years and nine months in one instance) and the degree of comfort afforded the patient.

The operative mortality rate for the series was 10 per cent.

CONCLUSION

The surgical excision of solitary, metastatic, malignant lesions of the lung is indicated in certain cases in which the primary tumor apparently has been completely removed and in which there is no evidence of further metastatic spread. Experience has shown that in a few instances survival for many years may be expected to follow such a procedure, while at other times the degree of palliation afforded makes the attempt justifiable.

ADDENDUM

Since the completion of this work, pulmonary resection for metastatic lesions has been performed in 6 more cases at the Mayo Clinic. The primary lesions in this group included 2 fibrosarcomas (chest wall), 1 osteogenic sarcoma, 1 hypernephroma, 1 adenocarcinoma of the uterus, and 1 adenocarcinoma of the maxillary antrum (cylindroma type). Pneumonectomy was carried out in 2 instances and lobectomy in four. Bronchial involvement was noted in 2 cases. Two patients have since died of recurrence of their malignant disease at eight months and one year, respectively. The remaining 4 patients are alive and have had no evidence of return of their disease for periods of eighteen months, eight months, eight months, and four months, respectively.

REFERENCES

1. Alexander, John, and Haight, Cameron: Pulmonary Resection for Solitary Metastatic Sarcomas and Carcinomas, Univ. Hosp. Bull., Ann Arbor **12**: 117-118, 1946; Surg., Gynec. & Obst. **85**: 129-146, 1947.

2. Effler, D. B., and Blades, Brian: Surgical Treatment of the Solitary Lung Metastasis, J. THORACIC SURG. **17**: 27-37, 1948.
3. Seiler, H. H.: Pulmonary Resection for Metastatic Malignancy, Thesis, Graduate School of the University of Minnesota, 1948, 142 pp.
4. Gerulanos, M.: Eine Studie über den operativem Pneumothorax in Anschluss an einen Fall von Lungenresection wegen Brustwandsarkom, Deutsche Ztschr. f. Chir. **49**: 497-536, 1898.
5. Sedillot: Quoted by Gerulanos.[4]
6. Meyer, Willy: Observations on Lung Suppuration and Its Treatment; a Brief Review of Personal Experiences and Clinical Impressions Obtained Within the Last Twelve Years, Arch. Surg. **6**: 361-425, 1923.
7. Diviš, Georg: Ein Beitrag zur operativen Behandlung der Lungengeschwülste, Acta chir. Scandinav. **62**: 329-341, 1927.
8. Torek, Franz: Removal of Metastatic Carcinoma of the Lung and Mediastinum; Suggestions as to Technic, Arch. Surg. **21**: 1416-1424, 1930.
9. Lilienthal, Howard: Pneumonectomy for Sarcoma of the Lung in a Tuberculous Patient, J. THORACIC SURG. **2**: 600-615, 1933.
10. Röpke, W.: Mehrjährige Heilung nach Operation eines Lungenkarzinoms, Zentralbl. f. Chir. **64**: 803-806, 1937.
11. Barney, J. D., and Churchill, E. D.: Adenocarcinoma of the Kidney With Metastasis to the Lung Cured by Nephrectomy and Lobectomy, J. Urol. **42**: 269-276, 1939.
12. Barney, J. J. D.: Twelve-Year Cure Following Nephrectomy for Adenocarcinoma and Lobectomy for Solitary Metastasis, J. Urol. **52**: 406-407, 1944.
13. Churchill, E. D.. Resection of the Lung, Surgery **8**: 961-991, 1940.
14. Cotton, B. H.: Differential Diagnosis of Primary and Metastatic Malignancy of the Lung, Am. J. Surg. **54**: 173-178, 1941.
15. Raine, Forrester: Metastatic Carcinoma of the Lung Invading and Obstructing a Bronchus, J. THORACIC SURG. **11**: 216-218, 1941.
16. Freedlander, S. O., and Greenfield, Jack: Hemoptysis in Metastatic Tumors of the Lung Simulating Bronchiogenic Carcinoma; a Report of Two Cases, J. THORACIC SURG. **12**: 109-116, 1942.
17. King, D. S., and Castleman, Benjamin: Bronchial Involvement in Metastatic Pulmonary Malignancy, J. THORACIC SURG. **12**: 305-315, 1943.
18. Brezina, P. S., and Lindskog, G. E.: Total Pneumonectomy for Metastatic Uterine Carcinoma, J. THORACIC SURG. **12**: 728-733, 1943.
19. Deming, C. L., and Lindskog, G. E.: Papillomatosis of Bladder and Entire Urethra; Infiltrating Cancer of Bladder. Late Pulmonary Metastasis. Successful Pneumonectomy, Tr. Am. A. Genito-Urin. Surgeons **37**: 39-50, 1944.
20. Blalock, Alfred: Recent Advances in Surgery, New England J. Med. **231**: 261-267; 293-300, 1944.
21. Tinney, W. S., and McDonald, J. R.: Pulmonary Metastasis of Carcinoma Diagnosed by Bronchoscopy, Minnesota Med. **28**: 554-558, 1945.
22. Edwards, A. T.: Carcinoma of the Bronchus, Thorax **1**: 1-25, 1946.
23. Mandeville, F. B.: Roentgen and Clinical Problems in So-called Solitary Metastatic Tumors in the Chest, Am. J. Surg. **71**: 669-675, 1946.
24. Massachusetts General Hospital: Case 33012, New England J. Med. **236**: 38-40, 1947.
25. Overholt, R. H., and Langer, Lazaro: A New Technique for Pulmonary Segmental Resection, Surg., Gynec. & Obst. **84**: 257-268, 1947.
26. Maier, H. C., and Taylor, H. C., Jr.: Metastatic Chorionepithelioma of Lung Treated by Lobectomy, Am. J. Obst. & Gynec. **53**: 674-677, 1947.
27. Rienhoff, W. F., Jr.: The Present Status of the Surgical Treatment of Carcinoma of the Lung, Ann. Surg. **125**: 541-565, 1947.
28. Sweet, R. H.: Quoted by Alexander and Haight.[1]
29. Dolley, F. S.: Quoted by Alexander and Haight.[1]
30. Carr, Duane: Quoted by Alexander and Haight.[1]
31. Samson, P. C.: Quoted by Alexander and Haight.[1]
32. Flick, J. B.: Quoted by Effler and Blades.[2]
33. Willis, R. A.: The Spread of Tumors in the Human Body, London, 1934, J. & A. Churchill, Ltd., 540 pp.
34. Blalock, Alfred: Quoted by Effler and Blades.[2]

DISCUSSION

DR. D. H. WATERMAN, Knoxville, Tenn.—Dr. Seiler has shown that isolated metastatic lesions in the lung are not uncommon. In bronchiogenic carcinoma, however, metastasis limited to the contralateral lung is relatively rare. I rise to report an instance in this latter

group, in which we were confronted with the problem of an apparent metastasis arising in the opposite lung of a patient on whom a pneumonectomy had been performed some five and one-half years previously (slides).

The patient is a 53-year-old white man whom we first saw in October, 1942, with elevation of the left diaphragm and a six months' history of weight loss, cough, and other typical symptoms of bronchiogenic malignancy. Bronchoscopy at that time revealed a squamous-cell carcinoma blocking the left lower lobe bronchus. Following removal of biopsy tissue, the left lower lobe aerated and the diaphragm descended to its normal position. In November, 1942, total pneumonectomy was performed on the left using individual ligation technique. There was no evidence of mediastinal metastases at operation. Dyspnea did not develop subsequently, so thoracoplasty was not performed. The patient was followed at three-month intervals, and apparently did well, showing no signs of recurrence. However, in March, 1949, as shown in this slide, a small rounded lesion 1¼ by 2 cm. appeared in the right upper lobe. We thought there was a possibility of recurrent malignancy, but with perhaps wishful thinking, hoped it might be of some other origin. After a trial period of bed rest, however, the lesion was seen to be slightly larger. In view of this, we decided we were dealing with metastatic tumor, and suggested exploration. We were rather reluctant, of course, in such an instance to propose surgery, realizing the potential risks involved in any operative attack on a single lung. Unable to find a similar experience reported in the literature, we gave considerable thought as to what type of procedure would be advisable, first considering a preliminary operation to promote pleural adherence in the area. We rejected this because of the limitations it imposed, and reached the conclusion that open thoracotomy would be the procedure of choice.

The next slide showing the roentgenogram taken just before surgery indicates further enlargement of the lesion.

The patient was operated upon on Sept. 10, 1948, under intratracheal cyclopropane. A posterolateral incision was made and the pleural cavity entered through the fifth intercostal space without division of either the fifth or sixth ribs. This approach was used so there would be as little interference as possible with the function of the remaining hemithorax. No adhesions were present. The right lung was kept fully inflated with positive pressure throughout the operation to insure adequate aeration. The lesion was found to be a firm, round tumor mass, somewhat smaller than a walnut, located in the posterior aspect of the right upper lobe just above the fissure. A wedge segmental resection was performed between clamps, removing about 2.5 cm. of lung tissue on either side of the tumor.

A fenestrated catheter was inserted along the gutter to a point just above the area of resection, and continuous suction instituted postoperatively for two days. Fortunately the postoperative course was uneventful and recovery took place without incident.

These color slides show the gross specimen and the microscopic appearance. The pathologist reported the tumor to be apparently a metastatic squamous-cell bronchiogenic carcinoma.

This last slide is the present situation six months after operation, showing some residual fibrosis in the area of the resected lesion. The man has had no evidence of difficulty since operation, and has returned to active business life; he is an ardent fisherman and hunter, and has taken up these sports as well.

I think I might say in conclusion that we are perhaps open to criticism for procrastinating in this case before proceeding to surgery. I believe we are justified in saying that the appearance of a circumscribed lesion in the lung following previously known carcinoma should always be considered a metastatic lesion until proved otherwise.

DR. JOHN ALEXANDER, Ann Arbor.—The patients and the surgeons who deal with this condition are confessed gamblers. Before deciding whether or not to remove the pulmonary metastatic lesion, a biopsy of the site from which the primary lesion was removed (if this site is relatively superficial and accessible) will indicate whether the primary lesion has been completely removed. But it is pure guesswork, apart from the thoroughness or lack

of thoroughness with which the body is explored for possible demonstrable metastases other than the obvious one in the lung, whether there are other metastases which are not demonstrable and which, if present, presumably cannot be removed.

Dr. Haight and I felt that it would be of interest if a follow-up were presented to you concerning the patients we reported upon in 1947 (slide). These are not grouped chronologically but according to the type of lesion and, incidentally, a few have been added since 1947. The largest group by far, in contradistinction to Dr. Seiler's patients, had sarcomas. The first group is of sarcoma, the second of carcinoma, and the last, a single case, is a cystoma of the ovary which microscopically was considered to be benign but which had metastasized to the lung. Two of the living patients have new metastases which are irremovable and, of course, thees patients will die. Among the whole group of 11 patients, 4 are dead, 2 will almost certainly die, and 5 are in excellent health with no sign or symptom of malignancy.

Our first and most interesting patient, and the one who convinced us that the gamble is worth while, is a woman who had a very malignant type of spindle-cell sarcoma of the median nerve, which was removed by Dr. Alexander T. Bunts at the Cleveland Clinic nine and one-half years ago. One year later a small lesion appeared in the right lower lobe; Dr. Bunts explored the forearm because of causalgia and found a benign fibroma without any evidence of recurrence. I removed the right lower pulmonary lobe and one year later the patient returned for a check-up examination because of cough; she had a large lesion in the left upper lobe. Ill luck had returned; more than one metastatic lesion had been present and, possibly, a great many. I decided, however, to remove the left upper lobe on the remote chance that it contained the only remaining malignant tissue; the patient is now perfectly well eight and one-half years after the second lobectomy.

The second patient is also of special interest; he had had two operations on his thigh for a myogenic sarcoma, the second of which was probably for an implantation lesion; before I removed the right upper lobe, I had biopsy specimens taken of the thigh—three deep slices to the femur from which 50 sections were prepared and no sarcoma cells were found. The reason for a strong suspicion of recurrence locally at the site of the primary lesion was that this patient had inadvisably been given very heavy doses of x-ray therapy following removal of the thigh sarcoma, and there was deep ulceration so that it was imposible to tell from inspection and palpation whether there had been a recurrence. But there was none and he is well and working, six and three-quarter years after operation, and without any sign of another metastatic lesion.

We have learned very little since our first patient of nine and one-half years ago as to what criteria, other than the obvious ones that occur to us all, are important with regard to a reasonable expectation of a cure or possibly of prolonged relief of distressing symptoms.

DR. G. N. J. SOMMER, JR., Trenton, N. J.—It is interesting to note that Weinlechner* in 1881 removed two metastatic tumors from the lung at the time of resection of a huge sarcoma of the bony thoracic wall. The patient died postoperatively. Krönlein in 1883,† removed a metastatic sarcoma in the lower lobe of the lung when operating for a recurrent primary tumor of a rib. The patient lived for six years and died of a further recurrence of the costal sarcoma without further apparent pulmonary lesions. In both these cases the metastatic tumors were definitely hematogenous and did not involve the lungs by continuity.

The pathologic basis on which metastatic tumors may be successfully treated has been laid by Schmidt and Muir. Schmidt‡ showed that in the presence of visceral carcinoma many tumor cells pass to the lungs. Most of these tumor emboli, however, do not survive or, if they do grow, remain of microscopic size and cannot be disclosed without very careful examination of the lungs. Furthermore, peripheral metastases arise, not from tumor emboli passing through the pulmonary capillaries, but from the pulmonary metastatic tumors, which may be the microscopic ones described. It is also from such microscopic pulmonary metastatic tumors that

*Wien. med. Wchschr. 32: 589, 1882.
†Berliner. klin. Wchschr. 21: 129, 1884.
‡Die Verbreitungswege der Karzinome, Jena, 1903.

recurrences arise after resection of apparently solitary metastatic tumors of the lung. Muir* emphasized the importance of tissue resistance to metastatic tumors in limiting their growth and spread. Willis† concurs in the views of Schmidt and Muir.

A case under the care of the speaker illustrates the views already outlined. The 52-year-old male patient had complained of thoracic pain for one year. Roentgenographic examination showed the lesion, which was thought to be of an inflammatory nature, involving the right seventh rib. It was explored with local anesthesia. Histologic examination disclosed an adenocarcinoma. Because of vague abdominal symptoms and the demonstration of several colonic diverticula, it was thought that the primary tumor was probably a minute one in the gastrointestinal tract. Roentgen ray therapy was administered to the costal tumor. After discussion of a similar case with Dr. I. R. Trimble of Baltimore, however, the seventh and the adjacent two ribs were widely resected. The patient lived for two years. Further studies failed to disclose a primary tumor. He died suddenly of gastrointestinal hemorrhage. The autopsy was performed in a mortician's establishment. The primary adrenal tumor was found above the right kidney. The fatal hemorrhage had come from an ulcer of the pyloric end of the stomach. Material for microscopic sections of the lung was taken from a caseous apical focus and foci considered to be pneumonic at the base of the right lung. The histologic sections of the second portion of lung, however, showed adenocarcinoma similar to that of the adrenal and rib. Numerous roentgenographic studies of the lungs had never shown evidence of metastatic tumor. No other gross secondary tumors were found in the post-mortem examination. Effler and Blades‡ have described a case in which a solitary pulmonary metastatic tumor was removed and later an apparently solitary one of the brain.

DR. ARTHUR AUFSES, New York.—I think there is one subject that has not been touched upon; that is the possibility that the solitary lesion that is seen in the lung after the patient has been known to have a carcinoma, may not be metastasis; it may be another primary tumor. That should be kept in mind in thinking about exploration for removal of a single lesion in the lung under such circumstances. We have recently had two patients one of whom had been treated for a number of years for a squamous-cell carcinoma of the lip, and who developed a solitary nodule in the lung. On removal of this lobe—we did a lobectomy because we felt that it was a metastasis—it was found to be a primary lesion of different nature from that of the lip, an adenocarcinoma. Another patient had had a carcinoma of the colon removed eight years previously, then a gastrectomy for carcinoma of the stomach two years previously, and then came in with a solitary lesion of the lung. A pneumonectomy was performed and the lesion in the lung was squamous-cell carcinoma, whereas the other two were adenocarcinomas. For that reason we feel that any solitary lesion must be considered to be possibly another primary carcinoma.

DR. WILLARD VAN HAZEL, Chicago.—I believe that the mesothelial metastatic lesions probably promise us more than the epithelial ones. We have had four patients with epithelial metastases, and only one is living, but she has other metastases. On the other hand we have six cases of sarcoma; the first was one that I reported not as a metastatic lesion but as a primary lesion of pulmonary osteoarthropathy in 1939. This girl had a grapefruit size mass in the chest which we removed; there was only a stalk about the size of a pencil which was fused with the fissures on the right side. This was reported as a fibroma, but the pulmonary osteoarthropathy returned in 1940. Little could be seen on the roentgenogram and because of the diagnosis of fibroma we did not suspect a recurrence, but there was nodulation at the hilus. On exploration we found nodes at the hilus and we did a resection, removing the lung in 1941. Since that time, three years ago, this girl has developed a lesion over the deltoid and we removed a similar tumor, undoubtedly metastatic, so the pneumonectomy did not cure her. Two years ago she had a popliteal tumor of similar character and it could be removed. She is still living and able to do things, although not in the best of health.

*Textbook of Pathology, ed. 4, Baltimore, 1936. William Wood & Company.
†Pathology of Tumors, St. Louis, 1948, The C. V. Mosby Company.
‡J. THORACIC SURG. 17: 27, 1948.

A second boy who had a sarcoma of the leg, an osteogenic sarcoma, removed nine years before, developed pain and swelling in the remaining ankle, and when the roentgenologist took the x-ray picture and saw that he had but one leg he suspected pulmonary osteoarthropathy and took a picture of the chest. He found a very dense shadow in the upper left lobe. We removed the upper lobe in 1941 and the patient has had no recurrence of touble and is entirely well.

We have had two other patients with sarcoma, one three years ago, one two years ago; both had sarcoma of the arm and had had recurrences and developed a lesion in the chest. Both have had lobectomies and are still well. We had another case on which I cannot tell you the final result; it was four years ago, and for two years he was well. The tumor was of enormous size and the original tumor was in the popliteal space. The last case is too recent; recurrence was present within a year after removal of an osteogenic sarcoma of the left leg. There is no local recurrence but she failed to appear at the dispensary for follow-up from last June until February, when this lesion was discovered. It had become of enormous size, but lobectomy with partial resection of the diaphragm was done.

I believe that probably sarcomas, because of their nature, being a low-grade disease as mentioned by the essayist, do offer more than the epithelial tumors.

DR. ADRIAN LAMBERT, New York.—I have one case that I think would be of interest. Three years ago I resected a 26-year-old girl's left upper lobe for a large globular adenocarcinoma that was four inches in diameter. We felt at the time that no lymph glands were involved; eight or ten were sent to the laboratory for section and were negative. We felt we were around the tumor until the paraffin sections came back and showed there were cells in one of the pulmonary veins. We therefore suspected that possibly she would develop metastases thereafter. Four months later she developed a lump on the thigh which I excised; it turned out to be just fibrous tissue. Eight months after this time, she developed a small, 1 cm. size nodule in the right lung. It was in the right upper lobe. Exploration for that was carried out one year after the original left upper lobe lobectomy and a right upper lobe lobectomy was performed. The tumor was exactly the same type of tissue as was seen in the original adenocarcinoma.

She has now gone two years and is living and well.

BRONCHIOGENIC CARCINOMA

I. A Pathologic Clinical Correlative Study of Full-Size Mounts From Operated Carcinomas

Francis J. Phillips, M.D., Clair E. Basinger, M.D.* (by invitation), and William E. Adams, M.D.
Chicago, Ill.

THE controversy among clinicians and pathologists regarding the pathogenesis of primary carcinoma of the lung stimulated one of us (W.E.A.) to make full-size mounts of representative cross sections of all tumors of the lung removed. This material has been collected from resected cases in this department over a period of nine consecutive years. The study represents at least three-year follow-up on all cases. An attempt has been made to correlate the type of tumor, the site of the tumor, and the size of of the tumor with clinical manifestations as demonstrated by history, physical findings, radio fluorographic interpretations, bronchoscopic examination, and exploratory thoracotomy. A cross section of the entire tumor has been studied in detail for variation in type of malignant cells. The type of cell has been studied in its relationship to the site and size of the tumor, the rapidity of growth, direct extension to contiguous tissues, and metastases to other organs. The tumors have been studied for variation of type of cell within the tumor. All these inherent characteristics of the tumors have been studied in relationship to the duration of symptoms and objective manifestations of the growths per se. No attempt has been made to grade the cell malignancy from the microscopic appearance of the cells within the individual types of tumors. The following tables with individual respective discussions give comprehensive evaluation of the correlations included here.

COMMENTS ON TABLE I

The clinical recognition of carcinoma of the lung is often very difficult. The existence of the tumor is not recognized often until the opportune time for favorable operation has passed. The symptoms bringing the patient to the clinic may be very bizarre and apparently unrelated to tumor of the lung. It is not rare for tumor of the lung to be found in routine x-ray examinations of patients being admitted to the hospital for other diseases. At this hospital the incidence of lung tumors of all types for all admissions both to the outpatient clinic and to the hospital is $\frac{6}{10}$ of 1 per cent.[1] In these examinations 4, or 10 per cent, of the aforementioned cases were discovered at the time of routine chest fluoroscopic admission examination for some other disease. Seven of the cases had no physical findings on regular physical examination. Twenty-five, or 62.5 per cent, of the 40 had some degree of hemoptysis. Any streaking of the sputum with blood was classified as hemoptysis. The number having cough and sputum was 32, or 80 per cent. Only 26 of the group had weight loss. This is a finding usually associated with carcinoma in any part of the body. Although 14 of the group

Read at the Twenty-ninth Annual Meeting of The American Association for Thoracic Surgery, New Orleans, La., March 29-31, 1949.

From the Department of Surgery of the University of Chicago. This work was supported in part by grants from the Douglas Smith Foundation for Medical Research and the Illinois Federation of Women's Clubs.

*Work done in conjunction with Senior Thesis.

TABLE I. INCIDENCE OF SYMPTOMS PREVIOUS TO DIAGNOSIS

SYMPTOMS	MONTHS				TOTAL WITH SYMPTOM
	1 TO 6	6 TO 12	12 TO 18	19 PLUS	
Hemoptysis	11	6	5	3	25
Cough and sputum	9	12	6	5	32
Pleuritic pain	2	8	0	0	10
Emaciation	9	8	6	3	26
Fever and night sweats	6	4	3	1	14
No symptoms	–	–	–	–	4
No physical findings	–	–	–	–	7

had fever and night sweats of varying degree only 1 of the cases was found to have tuberculosis at autopsy. As would be expected the greater number had specific symptoms recognizable within the one-year period previous to diagnosis. Although the peripherally located group represents only approximately 20 to 25 per cent of all bronchiogenic carcinomas, 18, or 45 per cent, of the resected tumors of this series were in this group. This is explained by the fact that some of these tumors were found on routine fluoroscopic examination before symptoms had developed. Ten of this group had pleuritic pain. The unreliability of these symptoms and physical findings is well demonstrated in the preceding table and discussion. This same experience has been observed by many other surgeons.[2, 3, 4]

COMMENTS ON TABLE II

TABLE II. LABORATORY OR OBJECTIVE EVIDENCE OF TUMOR

ROENTGENOGRAM	NUMBER	PER CENT
Tumor visualized	26	65
Atelectasis	27	67

The problem of recognizing early tumor of the lung in the roentgenofluorographic examination is a difficult one. The identification of a primary tumor of the lung is even less easy. A thorough review of the films on the aforementioned 40 patients knowing that they had carcinomatous lungs resulted in identifying only 26, or 65 per cent. That number is greater than the number originally recognized as tumor by the roentgenologist on routine initial examination. The observation of atelectasis was of little more help. Often atelectasis is observed distal to the site of a discrete tumor mass as a result of bronchial obstruction produced by the mass. The finding of atelectasis alone without other evidence of tumor is in itself not diagnostic of tumor of the lung. The x-ray examination, therefore, is valuable as a diagnostic aid primarily in so far as the particular tumor is discretely evident in the lung fields visualized, but it is often helpful as a suggestive indication of pulmonary pathology.

COMMENTS ON TABLE III

Gross recognition of a bronchiogenic tumor and biopsy is only partly successful in the centrally located tumors. The tumor may be anatomically centrally located, but be situated outside the bronchus and thus be unrecognizable through the bronchoscope. The experienced bronchoscopist can readily recognize the presence of a protruding or fungating carcinoma grossly. Biopsy must be utilized to identify the suspicious lesions. In this series 24 of the 26 with positive findings had biopsies. The remaining 2 recognized were diagnosed grossly.

TABLE III

BRONCHOSCOPIC EXAMINATION	NUMBER	PER CENT
Number examined	38	95
Positive endoscopically	26	65

For technical reasons biopsy was not done or the section was uninformative. In the hands of the skilled and experienced bronchoscopist the bronchoscope is very helpful. The diagnosis can frequently be made and the resectability of the tumor estimated since its location in the tracheobronchial tree can be determined with considerable degree of accuracy. Also, it is often possible to make pertinent observations regarding the mobility of the tracheobronchial tree that are helpful in surgical evaluation of the pathology.

COMMENTS ON TABLE IV

TABLE IV. INTRAPULMONARY LOCATION AND METASTATIC INCIDENCE

STATUS	PERIPHERAL	METASTASIZED	CENTRAL	METASTASIZED
Living	3	2	7	2
Dead	15	9	11	5
Totals	18	11	18	7

These data indicate that the incidence of metastases was greater in the peripheral tumors. The metastases are considered without reference to cause of death. The causes of death in these cases is of other importance than the study of the pathogenesis of the tumor because of the diverse causes of death in the various cases. That is, not all deaths were the result of the tumor or the operation per se. These data seem to support the observations of Tuttle and Womack.[5] The four cases of "so-called" adenomas are not included or considered in the interpretations because they are inherently slowly growing tumors even though some have proved to be capable of metastases. The tumor was located centrally in all 4 of the cases. In 1 case no metastases were demonstrable at operation, but later the patient was found to have metastases to the liver, and subsequently died of metastases. She had metastases to the brain. Also this type of tumor is obviously of more serious consequence than is often ascribed to it by many surgeons and pathologists. Graham and Womack have reported proved cases of malignant transformation of these tumors.[6]

COMMENTS ON TABLE V

TABLE V. TYPE OF CARCINOMA CELLS CORRELATED WITH SITE AND SYMPTOMS

SITE AND SYMPTOMS	SQUAMOUS WITH PEARLS (PER CENT)	SQUAMOUS WITHOUT PEARLS (PER CENT)	ADENO AND SQUAMOUS (PER CENT)	ADENOMATA (SLOW GROWING) (PER CENT)
Hemoptysis	60	66.6	32.2	75
Pain	20	33.3	32.2	25
Emaciation	66.6	56.6	88.8	100
Cough and sputum	80	83.3	77.7	100
Central	73.3	50	11.1	100
Peripheral	26.7	50	88.9	0

The adeno- and squamous-cell type, along with having the greater mortality, had the least number with hemoptysis, and with having the greatest percentage with emaciation, this group had the lowest percentage with pain. This group had the greatest number of peripherally located tumors. Hemoptysis was almost equally common in the two squamous-cell groups. The variation of pain and emaciation is not significant in those two groups. The squamous-cell group with pearls had the higher percentage of central tumors which is quite opposite to the adeno- and squamous-cell group, but similar to the adenomas or slower growing group of tumors. This latter group ranked highest in weight loss, cough, and sputum production, but equally low with squamous-cell group with pearls in pain. Since these two groups were more consistently located centrally it may be explained that there was less pleural involvement and therefore less associated pain with these tumors. It is important to note that cough and sputum were the most common or at least a very common symptom in all types of tumors. These symptoms may well be the first evidences of tumor, yet since the normal person coughs and raises sputum a significant part of the time they may well be ignored as a cardinal early sign of bronchial new growth. It is important, therefore, to give serious consideration to cough and sputum when they are mentioned by the patient.[7]

COMMENTS ON TABLE VI

TABLE VI. SUMMARY OF PATHOLOGIC FINDINGS AND PHYSICAL STATUS

TYPE OF CARCINOMA CELL	NO. OF CASES	LOCATION		SIZE			METASTASIZED		PHYSICAL STATUS			
		CENTRAL	PERIPHERAL	LARGEST (CM.)	SMALLEST (CM.)	AVERAGE (CM.)	NO.	PER CENT	LIVING AND WELL	PER CENT	DEAD	PER CENT
Squamous cell with pearls	15	11	4	7.0	0.7	3.24	6	40	5	33.3	10	66.6
Squamous cell without pearls	12	6	6	5.1	2.0	4.25	6	50	3	25	9	75.0
Adeno and squamous cell	9	1	8	9.5	3.0	5.55	7	77.7	2	22.2	7	77.7
Adenomas	4	4	0	6.0	1.6	3.27	2	50.0	2	50.0	2	50.0

The squamous-cell carcinomas predominate in this series by 67.5 per cent of the total tumors. The number with pearls was greater by three than the number without pearl formation. In the squamous-cell group both with and without pearls 62.9 per cent were centrally located. In the centrally located tumors 77.2 per cent were squamous-cell carcinoma. The squamous-cell type with pearls occurred in 64.7 per cent of the centrally located squamous-cell carcinomas. However, considering the entire squamous-cell group both centrally and peripherally located the squamous-cell carcinomas with pearls occurred in 15 of the 27 cases as against 12 without pearls or a ratio of 5 to 4. The 9 cases having adeno- and squamous-cell type carcinoma cells present in the same tumor represent only 22.5 per cent of the entire series. In this group only 1 was located centrally or 10 per cent of the group. Squamous cells were found in all of the cases excluding the adenomas. When considered with the inoperable group of lung carcinomas,

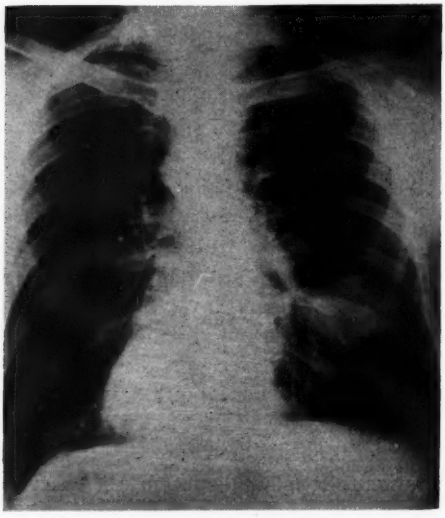


Fig. 1 (*A* to *C*).—Unit No. 308221, male, aged 45 years. Squamous-cell peripheral tumor with pearl formation. No metastases. Living.

Fig. 1, *A*.—Roentgenogram of chest previous to operation.

Fig. 1, *B*.—Photograph of tumor in cross section.

this figure of the incidence of squamous cells is significant. The "so-called" adenomas or slower growing carcinomas were all centrally located. They represent 10 per cent of the cases of the entire operated series.

Metastases had occurred in 18 of the series or 65 per cent of the total at the time of operation. Within the groups individually considered the incidence of metastases varied from the over-all percentage widely. In adeno- and squamous-cell grouping the 77.7 per cent metastases within the group represents only 17.05 per cent of the metastases of the entire series. This is the highest percentage of any single group. The incidence in the squamous-cell groups was 11, or 27.5 per cent. Two cases with metastases occurred in the adenoma group. One of these patients had continued a relatively normal life for a period of two years in spite of a proved metastasis to the liver found and biopsied during an abdominal operation two years after the primary tumor had been resected in the lung. This patient, however, died of widespread metastases three years later. Cases have

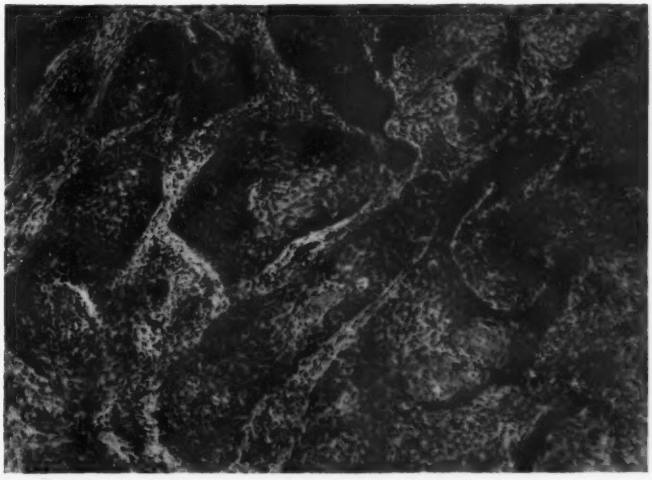


Fig. 1. *C.*—Photomicrograph of tumor showing pearl formations.

been reported of these tumors remaining intact and apparently dormant for many years and then becoming obviously malignant.[6] In the 19 cases with evidence of metastases the anatomic site of the primary tumor was peripheral in the lung in 10 and central in 9. All of the patients with metastases from peripherally located tumors are dead. There are only 6 of the patients dead from the group with centrally located tumors. Comparing these numbers with those of the entire series 28, or 70 per cent, of the resected cases were dead at the time of the study. Since 55 per cent of the tumors were centrally located the greater number of deaths has occurred in the patients with centrally located tumors. This figure, however, is obviously misleading since the study of each individual case reveals that a definite number of the deaths was not directly caused by the tumor, but was either operative deaths or deaths from other causes. It is concluded then, that in this study the incidence of metastases is informative, but the mortality rate is not significant to the analytic correlative study itself.

TABLE VII. SQUAMOUS CELL WITH PEARLS

UNIT NO.	SITE	AGE (YR.)	SEX	TUMOR SIZE (CM.)	HEMOPTYSIS (MO.)	PAIN (MO.)	FEVER AND NIGHT SWEATS (MO.)	EMACIATION (LB.)	EMACIATION (MO.)	COUGH AND SPUTUM (MO.)	METASTASES	PHYSICAL STATUS: LIVING AND WELL	PHYSICAL STATUS: DEAD
114754	P	45	M	2.5 by 1.8	18	None	18	20	18	18	Hilar nodes		1
252425	C	56	M	3.8 by 2.0	2	5	2	15	2	6	Left adrenal		1
318201	C	47	M	3.2 by 2.5	8	None	8	None		8	Hilar nodes		1
286505	C	56	M	1.8 by 1.2	12	12	6	14	12	18	None		1
245319	C	56	M	3.0 by 2.0	3	None	None	15	3 yr.	3	None		1
308221	P	45	M	4.0 by 3.2	None	None	None	None		None	None	1	
343491	C	58	M	6.2 by 5.0	None	None	None	40	11	5	None	1	
278817	C	42	M	2.5 by 1.8	15	None	15	25	15	15	Mediastinum		1
342938	C	40	M	5.0 by 2.0	6	None	18	15	6	6	None	1	
341646	C	58	M	6.2 by 5.0	4	None	None	90	18	6	None	1	
334552	C	59	M	5.5 by 3.0	3	9	3	46	8	7	Mediastinum		1
10897	C	48	M	3.3 by 3.2	None	None	None	None		9	Brain		1
323993	P	58	M	0.5 by 0.7	None	None	None	4	2	None	None		1
370186	C	59	M	9.5 by 4.5	None	None	None	None		12	None	1	
172703	P	57	M	5.0 by 4.5	None	None	None	None		None	None		1

Number of cases	15	Number located centrally	11	Number located peripherally	4
		Metastasized	5	Metastasized	1
Oldest patient	54	Youngest patient	42	Average age	52.8 yr.

The size of the tumor appears to have no relation to the incidence of metastases. In fact, the largest tumor resected, No. 256381, had no demonstrable metastases. The patient died of cardiac failure within a short period of time following the operation. It may be significant that this patient had no symptoms or physical findings preoperatively and the tumor had both adeno and squamous cells within its stroma. The data on size of the tumor is of primary interest in demonstrating the size of the individual tumor itself exclusive of tissue reaction around the lesion. It has been observed in this study that a chronic pneumonitis surrounding a tumor may mislead both the roentgenologist and the thoracic surgeon as well in judging the size of the tumor even at the operating table.

COMMENTS ON TABLE VII

The average age of patients in this group was 52.8 years. The average gross dimensions of the tumors were 3.8 cm. in the largest diameter and 2.94 cm. in the shortest diameter. Five of this group are still alive, or 33.3 per cent. One of the 5 who is living came to surgery as an incidental finding of carcinoma. He had had no symptoms or physical evidence of carcinoma. The tumor was larger than the average of the group, but smaller than the average of the entire series.

Fig. 2 (*A* to *C*).—Unit No. 10897, male, aged 48 years. Squamous-cell tumor with metastases to brain. Dead.

Fig. 2, *A*.—Roentgenogram of chest previous to operation.

One of the other patients who is still living had no symptoms, but had had a forty pound weight loss in the previous eleven months. The tumor was as large as the average of the series. The tumors in the patients living were located, one peripherally and four centrally. None have evidence of late metastases. The remainder of the cases had no significant correlative informative data.

Two of this group had had no symptoms or had no physical findings, yet their tumors were well above the average of the group in size. One is still living

after five years and one did not survive. One patient, No. 341646, had had mild hemoptysis for only four months, yet he had lost ninety pounds in weight over a period of eighteen months. The only other symptoms were cough and sputum for six months previous to diagnosis.

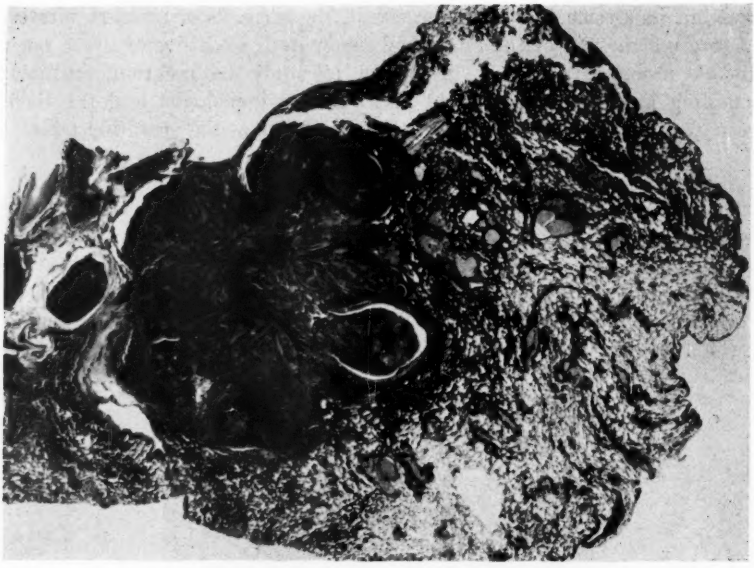


Fig. 2, *B*.—Photograph of tumor in cross section of resected lung.

Fig. 2, *C*.—Photomicrograph showing squamous-cell carcinoma with pearl formation.

COMMENT ON TABLE VIII

The average gross dimension of the tumors in this group was only slightly larger than in the previous group, but the variation of size within the group was less. In this group the peripheral tumors had within their number the

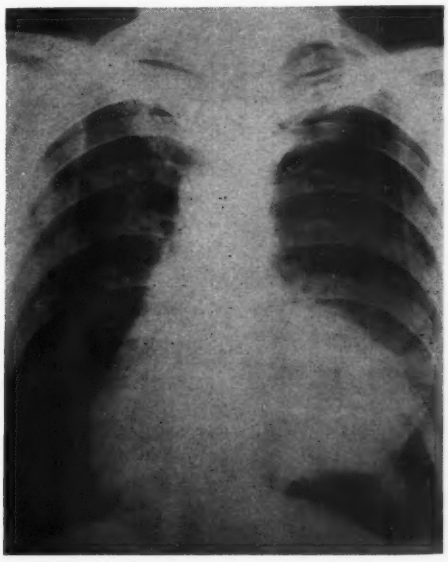


Fig. 3 (*A* and *B*).—Unit No. 294639, male, aged 47 years. Squamous-cell peripheral tumor without pearls. Living. No metastases.
Fig. 3, *A*.—Roentgenogram of chest previous to operation.

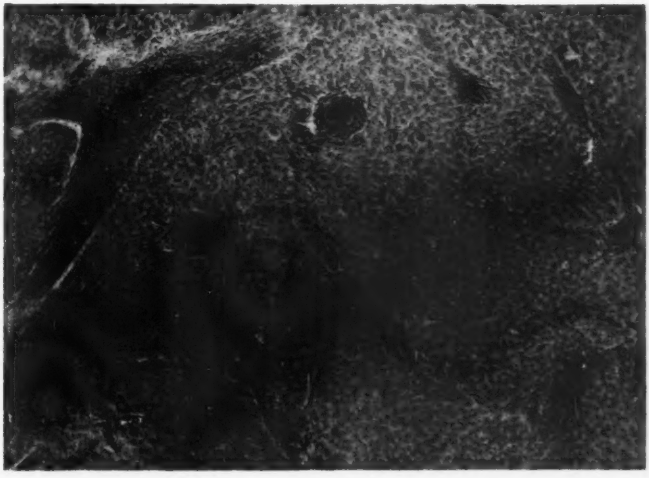


Fig. 3, *B*.—Photomicrograph of section without evidence of pearls.

TABLE VIII. SQUAMOUS CELLS WITHOUT PEARLS

UNIT NO.	SITE	AGE (YR.)	SEX	TUMOR SIZE (CM.)	HEMOPTYSIS (MO.)	PAIN (MO.)	FEVER AND NIGHT SWEATS (MO.)	EMACIATION LB.	EMACIATION (MO.)	COUGH AND SPUTUM (MO.)	METASTASES	PHYSICAL STATUS LIVING AND WELL	PHYSICAL STATUS DEAD
166063	C	42	M	2.0 by 2.0	2	None	2	20	12	2	Subcarinal node	1	
191716	C	58	M	4.5 by 2.5	9	None	2	10		9	Mediastinum		1
246006	P	51	F	7.5 by 3.8	None	None	None	15	2	None	None		1
243218	C	60	M	5.1 by 3.7	2	None	None	25	13	24	None		1
294639	P	47	M	6.6 by 6.9	None	None	None	46	18	18	None	1	
320031	P	44	F	5.1 by 3.7	None	8	None	None		2	None		1
341193	P	54	M	2.0 by 3.0	7	None	7	None		12	Hilar nodes		1
349403	C	64	M	1.5 by 2.2	None	10	None	25	12	10	Hilar nodes		1
360632	P	65	M	1.5 by 2.0	6	None	None	19	6	6	Mediastinum		1
337620	C	64	M	5.0 by 4.4	3 wk.	None	None	None		None	None		1
328415	P	64	M	4.0 by 1.5	3 wk.	3	None	None		12	Hilum and liver		1
240691	C	62	M	1.5 by 3.9	16	16	16	None		16	None	1	

Number of cases	12	Number located centrally	6	Number located peripherally	6
		Metastasized	3	Metastasized	3
Oldest patient	65	Youngest patient	42	Average age	57 yr.

TABLE IX. ADENO AND SQUAMOUS CELLS

UNIT NO.	SITE	AGE (YR.)	SEX	TUMOR SIZE (CM.)	HEMOPTYSIS	PAIN (MO.)	FEVER AND NIGHT SWEATS	EMACIATION (LB.)	EMACIATION (MO.)	COUGH AND SPUTUM	METASTASES	PHYSICAL STATUS LIVING AND WELL	PHYSICAL STATUS DEAD
233314	P	62	M	7.0 by 5.0	1 yr.	None	None	25	12	12 mo.	Right kidney		1
234309	P	50	M	5.0 by 6.0	None	2	None	16	2	12 mo.	Chest wall		1
256381	P	55	M	9.5 by 7.5	None	None	None	40	4	None	None		1
240063	P	69	F	2.0 by 3.0	None	None	None	None		3 yr.	Mediastinum		1
359364	P	62	M	6.2 by 4.0	None	None	None	7	1	None	Mediastinum		1
321365	P	57	M	6.2 by 3.0	2 wk.	None	None	35	3	2 wk.	Pericardium		1
299507	P	44	M	4.2 by 3.8	None	7	1 wk.	20	8	12 mo.	Mediastinum		1
340966	P	57	M	3.0 by 2.5	None	None	12 mo.	15	12	10 mo.	None	1	
342015	C	50	M	4.2 by 3.5	12 mo.	12	12 mo.	35	12	12 mo.	Pericardium	1	

		Number located centrally	1	Number located peripherally	8
Number of cases	9	Metastasized	1	Metastasized	6
Oldest patient	69 yr.	Youngest patient	44	Average age	55.7 yr.

Fig. 4 (*A* to *D*).—Unit No. 35964, male, aged 62 years. Adeno- and squamous-cell peripheral tumor with intermediate transition cell areas.
Fig. 4, *A*.—Roentgenogram of chest previous to operation.

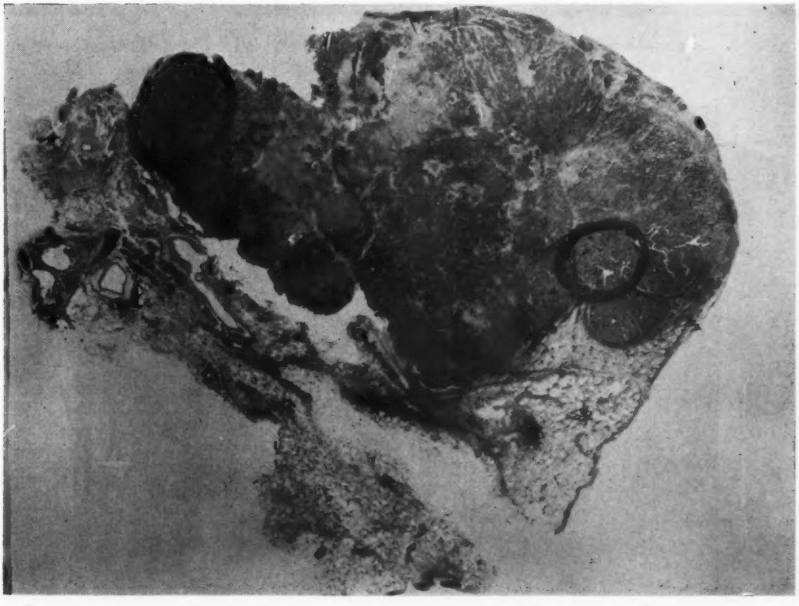


Fig. 4, *B*.—Two separate areas with adeno and squamous cells in each.

larger sized lesions. In the previous group one patient with a centrally located tumor had the largest sized lesion and had as the only symptom cough and sputum for a period of one year previous to diagnosis. There was no signifi-

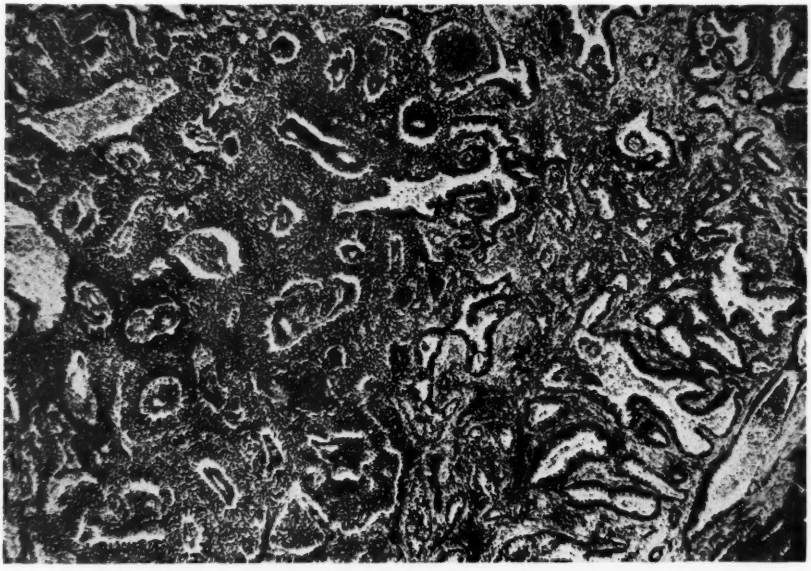


Fig. 4, *C*.—High power photomicrograph showing transition between two types of carcinoma cells.

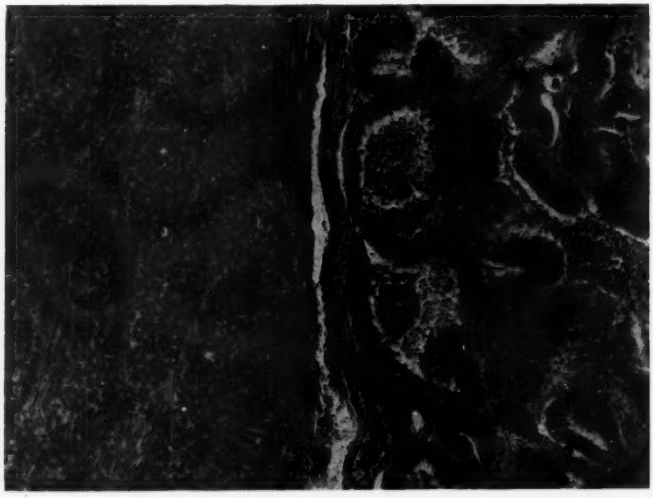


Fig. 4, *D*.—Low power photomicrograph of area with adeno- and squamous-cell structures contiguous.

TABLE X. ADENOMATA OR SLOWER GROWING CARCINOMA

UNIT NO.	SITE	AGE (YR.)	SEX	TUMOR SIZE (CM.)	HEMOPTYSIS	PAIN	FEVER AND NIGHT SWEATS	EMACIATION (LB.)	EMACIATION	COUGH AND SPUTUM	METASTASES	PHYSICAL STATUS: LIVING AND WELL	PHYSICAL STATUS: DEAD
226523	C	33	F	1.6 by 1.8	4 mo.	None	None	20	2 yr.	5 yr.	None	1	
243282	C	62	F	3.5 by 1.5	None	11 mo.	None	30	18 mo.	18 mo.	Bone marrow		1
165962	C	24	M	6.0 by 4.0	6 yr.	None	8 yr.	18	5 mo.	10 yr.	None	1	
232383	C	34	F	2.0 by 2.0	10 yr.	None	None	10	10 yr.	10 yr.	Liver and brain		1
Number of cases				4	Number located centrally			4		Number located peripherally		0	
							Metastasized	2					
Oldest patient				62	Youngest patient			24		Average age		38.2 yr.	

cance as to variation in the metastatic incidence in the two groups. Two of the patients in this group had had hemoptysis for only three weeks previous to diagnosis. One of the patients, No. 328415, had metastases to the liver and to the lung hilum, yet he had no weight loss. Neither patient survived. One of the three patients, No. 294639, who is still living, had had a weight loss of forty-six pounds over a period of eighteen months. He had had no pain. His tumor was classified as peripheral.

COMMENT ON TABLE IX

This group had the greatest number of cases with the tumor in the periphery. These were the fewest with hemoptysis. The weight loss was somewhat greater in this group. All but 2 of the cases had metastases either to contiguous organs or in one case to the kidney, No. 233314. This group carried the highest mortality on a percentage basis. The average size of the tumors in their greatest dimensions was 5.3 by 3.2 cm. The largest tumor occurring in the entire series was in this group, No. 25C381. This tumor had not metastasized. The patient did not survive. This group had the greatest number of metastases to the pericardium. The only metastases to the chest wall occurred in this group. One case in this group, No. 359364, is especially interesting in that the tumor was peripheral with both adeno- and squamous-cell areas adjacent to each other with an area of transition cells in between as illustrated in Fig. 4.

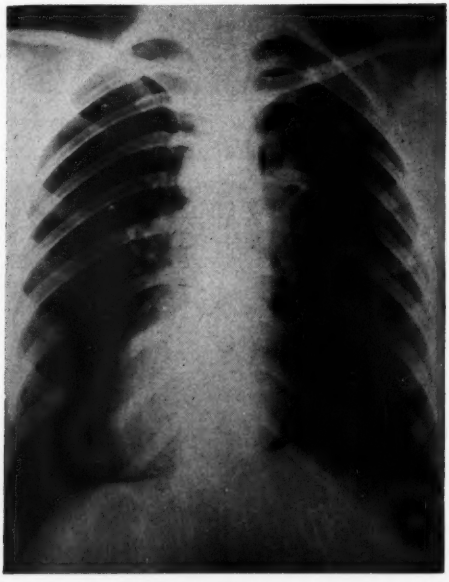


Fig. 5 (*A* to *C*).—Unit No. 232383, female, aged 24 years. Adenoma or slow growing carcinoma of lung with metastases to liver and brain. Dead.
Fig. 5, *A*.—Roentgenogram of chest previous to operation.

COMMENT ON TABLE X

This group of slower growing carcinoma represents 10 per cent of the cases in the study. One of the group had an early metastasis to the bone marrow of

the spine. Another one of the group, No. 232383, is of particular interest because of long treatment and clinical course. The tumor was first discovered in 1933. The patient was observed for some period of time. In 1935, she was given

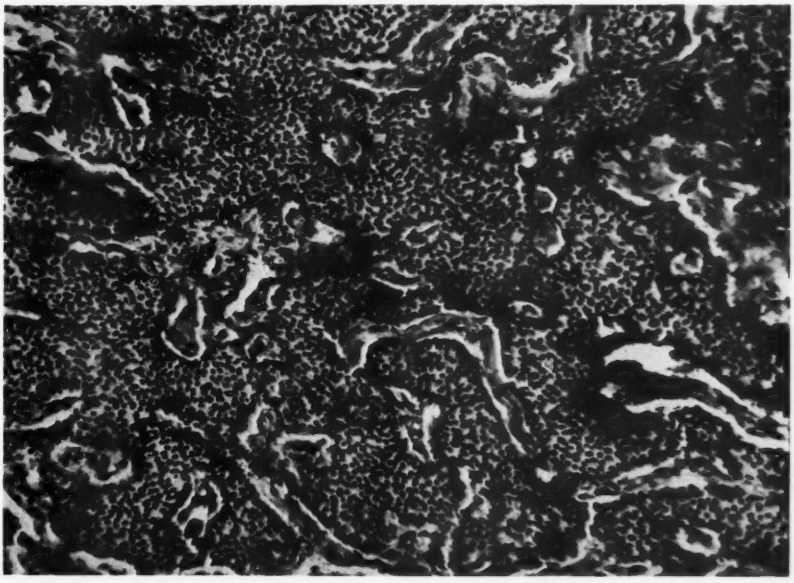


Fig. 5, *B*.—Photomicrograph of primary tumor in lung.

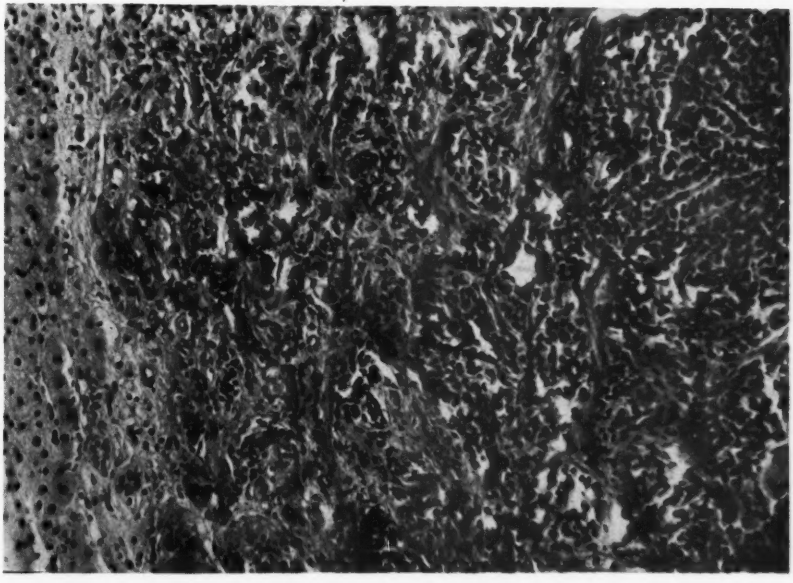


Fig. 5, *C*.—Photomicrograph of liver metastasis.

x-ray therapy to the tumor through the chest wall. The x-ray evidence of the tumor disappeared. However, the mass reappeared approximately eight years later. At that time, Oct. 14, 1943, a right bilobectomy was performed. Postoperative course was uneventful. She was apparently relieved of lung symptoms. Two years later, or 1945, a pelvic operation was performed through the abdomen. On exploration nodules were demonstrable in the liver. Microscopic section of these nodules revealed a morphologic picture like that of the tumor removed from the lung two years previously. She survived until June, 1948, at which time she died with generalized metastases including the brain. These 4 cases were included in this series because of the similarity of symptoms to those of the more rapidly growing carcinomas. The main difference in the two types of tumors appears to be in the rate of growth.

DISCUSSION

This is believed to be the first such correlative study made of cross sections of resected lung carcinoma. We believe that the study is peculiar in that it demonstrates rather unequivocally that many of the former concepts regarding the growth, metastases, and microscopic characteristics of carcinoma are no longer tenable in dealing with these tumors of the lung.

The evidence presented in this paper that any combination of cell types may exist in the same tumor belies many of the previous beliefs that a particular cell type has a predilection for some specific area of lung tissue. This study of entire sections of tumors after resection has been very illuminating. Squamous cells with pearls were not found in the same tumor with adenocarcinomatous type cells. This may be indicative of growth phases, but there is no good proof that coincidence is not the correct explanation. This general finding is in close agreement with the concept of Graham and others that these tumors are really all carcinoma.[8, 9] Their unpredictable operability is again demonstrated. It is of special interest that we found no pure adenocarcinoma in any of these cases. One case had both adeno and squamous cells in close proximity to each other with a physical merging of one into the other (Fig. 4).

The finding of a greater number of metastases in the peripheral tumors is again an indication of failure of early recognition of the tumor. Proper clinical evaluation of mass chest x-ray examinations will reveal these apparent symptomless carcinomas in their early phases before metastasis or direct extension has taken place. The higher mortality rate of the peripheral tumors may well be attributed to late recognition and consequent more or less heroic surgical treatment. That the peripheral tumors are more malignant or are more consistently one type of tumor is a theory that is not substantiated in our series. Our study appears to indicate that the centrally located tumor has the lower metastasis rate and the lower death rate. We believe, however, that these findings stem from the fact that the central tumor presents symptoms earlier and is consequently removed before sufficient time has elapsed to allow metastasis to take place, and not because the peripheral tumor is more malignant. Ten of the 18 peripheral cases were of a squamous-cell type and 8 were adeno-squamous-cell type. Yet 11 of the 18 metastasized. Out of that 11, 6, or 54.5 per cent, of the metas-

tases came from the adeno-squamous type. Only 2 of these 6 had pain. Only 3 had hemoptysis. Two of the 3 had hemoptysis for one year or more. This would appear to indicate the presence of a growing tumor for a long period of time. One had hemoptysis only two weeks and yet that tumor was one of the largest of all types resected.

The potential malignancy of the so-called adenoma is further substantiated in 2 of the 4 cases presented. The death rate and metastasis rate were both 50 per cent. One metastasized to the brain and one to the spine, thus following common carcinoma metastatic patterns. Although there may be some plausible debate as to the cell origin and growth rate there is little doubt of the ultimate course of the tumor. Our cases and cases reported by other surgeons previously cited in this paper give convincing proof of the malignant nature of the so-called adenoma. One of us previously ascribed the term "malignant adenoma" to this type of tumor.[10] Now it appears that it may be prognostically sagacious to consider them carcinoma in general and accord them the serious respect given carcinoma of the lung. The ineffectiveness of x-ray therapy is demonstrated by our patient, No. 232383, who had massive irradiation yet she died of metastasis to the brain and liver. One patient with a squamous-cell carcinoma with pearl formation had x-ray evidence of a large tumor of the chest for a period of three years, yet there were no symptoms. He died of cardiac complications a few weeks after resection. Complete post-mortem examination revealed no metastases. Comparing the adenoma, so-called, with this proved case of carcinoma, it is difficult to ascribe less serious significance to the adenoma groups.

The time of diagnosis of the lung tumor appears to be of more prognostic significance than the type of cell found in the tumor or its location in the lung.

CONCLUSIONS

1. A study of 40 resected carcinomas of the lung has been made.

2. Squamous-cell and adeno-cell carcinoma have been demonstrated immediately adjacent within the same tumor mass.

3. Squamous-cell carcinomas with and without pearl formation were found in 36 individual tumors. No pure adeno type carcinoma cell tumors were found.

4. Two proved cases of metastasis of a so-called adenoma were studied and discussed.

5. No correlation between type of tumor cell or location of tumor within the lung and the prognosis was demonstrable in this study.

6. Lung carcinoma occurred almost six times more frequently in men than in women.

REFERENCES

1. Block, Robert G., and Tucker, W. B.: The Indispensability of Routine X-ray Examinations of the Chest in a General Clinic, Am. Rev. Tubere. **50**: 405, 1944.
2. Gibbon, John H., Jr., Clerg, Louis H., Herbut, Peter A., and De Turek, John J.: The Diagnosis and Operability of Bronchiogenic Carcinoma, J. THORACIC SURG. **17**: 419, 1948.
3. Block, Robert G., Adams, W. E., Thornton, Thomas F., and Bryant, Edmond J.: Difficulties in the Differential Diagnosis of Bronchiogenic Carcinoma, J. THORACIC SURG. **14**: 83, 1945.

4. Brewer, Lyman A., III, Jones, Wilfred M. G., and Dolley, Frank S.: Nonmalignant Intrathoracic Lesions Simulating Bronchiogenic Carcinoma, J. THORACIC SURG. **17**: 439, 1948.
5. Tuttle, W. M., and Womack, Nathan A.: Bronchogenic Carcinoma: A Classification in Relation to Treatment and Prognosis, J. THORACIC SURG. **4**: 125, 1934.
6. Graham, Evarts A., and Womack, Nathan A.: The Problem of the So-called Bronchial Adenoma, J. THORACIC SURG. **14**: 106, 1945.
7. Graham, Evarts A.: Bronchiogenic Carcinoma, Surg., Gynec. & Obst. **88**: 129-131, 1949.
8. Womack, N. A., and Graham, E. A.: Mixed Tumors of the Lung, Arch. Path. **26**: 165, 1938.
9. Rabinovitch, Jacob, Hochberg, Lew A., and Lederer, Max.: Primary (Bronchiogenic) Carcinoma of the Lung, J. THORACIC SURG. **9**: 332, 1940.
10. Adams, W. E., Steiner, P. E., and Block, R. G.: Malignant Adenomma of Lung Carcinoma-Like Tumors With Long Clinical Course, Surgery **11**: 503-526, 1942.

DISCUSSION

DR. JEROME HEAD, Chicago.—A great many years ago I had the opportunity of studying at the Mayo Clinic cell type and degree of malignancy, and Dr. McCarty, who was a good deal of an iconoclast and a tremendously imaginative person, was interested in asking why in one individual you have a rapidly growing tumor and in another individual a slowly growing tumor. He was interested in the resistance of the body to carcinoma. I think we have a tendency to approach the carcinoma problem from the wrong angle, considering these tumors as entirely isolated from the host, and as entirely uninfluenced by the host. It is quite conceivable to me that we all, at one time or another, have many carcinomas but that we are able to overcome them; we have a high resistance to the efforts of the cells to become autonomous. Perhaps the logical approach to the carcinoma problem is to increase the resistance of people to carcinoma rather than attempt to cure the occasional case where the carcinoma gets out of hand. I think, therefore, that when we talk about types of carcinoma, types of cells, grades of carcinoma, rapidity of growth, we should ask why does this carcinoma grow rapidly in this person, and consider the host as an important factor in the carcinoma problem.

DR. F. J. PHILLIPS.—I am very sorry that Dr. Graham is not here to discuss this paper. It was the stimulation of his studies and interpretation that stimulated Dr. Adams to start this work originally. We appreciate Dr. Head's speculations and discussion. Certainly in the light of what has been said about another type of carcinoma, adenomatosis, there may well be something to the individual's resistance to the tumor. There are others of us who feel somewhat the same way. Why, we do not know specifically.

Further discussion of the conclusions is not indicated. We have presented these studies as evidence of what may be found if the entire tumor is studied in cross section, and we believe that the sections speak for themselves.

BRONCHIOGENIC CARCINOMA

II. The Correlation of Pathologic Characteristics and Clinical Manifestation in Unresectable and Unexplored Post-mortem Lung Tumors

George M. Bogardus, M.D. (by invitation), Kalispell, Mont., and William E. Adams, M.D., and Francis J. Phillips, M.D., Chicago, Ill.

GRAHAM[1] has emphasized the need for continued study of carcinoma of the lung in order to extend knowledge and to improve the rate of cure. A study of the resected tumors of the lung has been made in this clinic by Phillips, Basinger, and Adams.[2] As a supplement to the paper by Phillips and associates this paper is concerned with information obtained from a study of carcinoma of the lung which was explored but found to be nonresectable, and carcinoma of the lung not operated upon but found at autopsy.

Adler[3] stated that perhaps Morgagni (1682-1772) was the first to publish the results of autopsies that might be diagnosed as cancerous. Following the fundamental discovery of Schwann, histology assumed a dominant role in pathology. According to Ewing,[4] the earliest microscopic studies of lung tumors were by Landhans, Marchiafava, and Malassez.

From a histologic standpoint, Adler assigned the majority of cases to the carcinoma group, and it is probable that present day pathologists would limit even further his group of sarcomas in which were the spindle and round cell forms now considered by some to be variants of carcinoma.[5] Under carcinoma simplex he included squamous and alveolar types. A second large group was composed of cylindric cells. He makes no mention of behavior of the tumor with respect to the cell type.

In Table I is shown clinical data pertinent to the age, sex, and symptomatology of the explored but nonresected group. It is apparent that men outnumber women about 5 to 1. The average age was 52 years and symptoms of cough, weight loss, sputum, chest pain, dyspnea, and hemoptysis were predominant in this group. It might be pertinent to note that the symptoms commonly associated with carcinoma of the lung occur in the advanced stages of the disease. Without wishing to discourage further investigation and attempts at therapy in this group, however, there is evidence that these tumors may be detected prior to the onset of symptoms by means of fluoroscopy and x-ray examination. This has been ably pointed out by Bloch and Tucker[6] and by Adams.[7]

Several studies of the cytology and behavior of carcinoma of the lung have been made in recent years, for example, Boyd,[8] Fried,[9] Karsner,[10] Weller,[11] Gebauer,[12] and Koletsky.[13] There has been relatively little emphasis upon the correlation of clinical behavior with the cell types. Notable among these attempts, however, was the work of Koletsky[13] who concluded that "the histologic

From the Department of Surgery of the University of Chicago.

This work was supported in part by a grant from the Illinois Federation of Women's Clubs.

Read at the Twenty-ninth Annual Meeting of The American Association for Thoracic Surgery, New Orleans, La., March 29-31, 1949.

classification of primary carcinoma of the lung may be correlated with essential differences in the growth, dissemination and prognosis of each tumor. The small cell carcinoma is a highly malignant tumor which offers a poor prognosis. Usually primary at the hilus of the lung, it readily invades the postero-superior mediastinum and metastasizes extensively, with special tendency to widespread extension through the lymphatic system. The tumor occurs in younger persons, and there is a short rapid course without notable remission. The squamous carcinoma is slowly growing, locally invasive, and relatively non-metastasizing growth accompanied by infection, necrosis and cavity formation. Involvement of lymph nodes other than the regional and tracheobronchial nodes is infrequent. This type of carcinoma, particularly a growth involving the hyparterial bronchi of the lower lobe offers the most favorable prognosis for complete resection. In cases of adenocarcinoma surgical intervention is less favorable, since the tumor, while locally invasive, shows more frequent and more extensive lymph node involvement and metastasizes injuriously by way of the blood stream." That this opinion is not unanimous at present is shown by two recent articles in the JOURNAL in which there seemed to be disagreement as to the value of the cytologic data in estimating prognosis.[14, 15]

TABLE I. THIRTY-SIX CARCINOMAS OF THE LUNG EXPLORED BUT NOT RESECTED

Men	30
Women	6
Average age (yr.)	52
Symptoms	
Cough	32
Weight loss	31
Sputum	27
Pain	27
Dyspnea	23
Hemoptysis	20
Anorexia	16
Fever	12
Night sweats	12
Average of longest symptom (mo.)	7
Average weight loss (mo.)	21

Adams[14] reported that "the cell type of carcinoma found by microscopic examination is the most important single consideration in estimation of prognosis after a resection. If the growth is undifferentiated or oat-cell carcinoma in type, less than a year of life may be expected. Of 15 patients now living and well beyond one year, 12 had epidermoid carcinoma, 2 had adenocarcinoma, and 1 undifferentiated carcinoma." In contrast with this statement is the report of Neuhof and Aufses[15] that "the microscopic features of cancer of the lung bear no significant relation to the ultimate prognosis."

Table II summarizes some of the pathologic information on our group of nonresected cases. It will be seen that the majority of these tumors fall into two groups, the undifferentiated, and the nonkeratinizing squamous variety. A much smaller group is composed of mixed forms containing more than one cell type, for example, both adenocarcinoma and nonkeratinizing squamous may be present. Of the bronchoscopic specimens, 9 were nonkeratinizing squamous

and 4 were undifferentiated, while 1 was reported as a basal cell tumor and 1 was a mixed form. The remainder had been bronchoscoped by outside doctors and their slides were not available for study. The biopsies removed at thoracotomy were found to be undifferentiated in 11, nonkeratinizing squamous in 5, a mixed type in 4, and adenocarcinoma in 1.

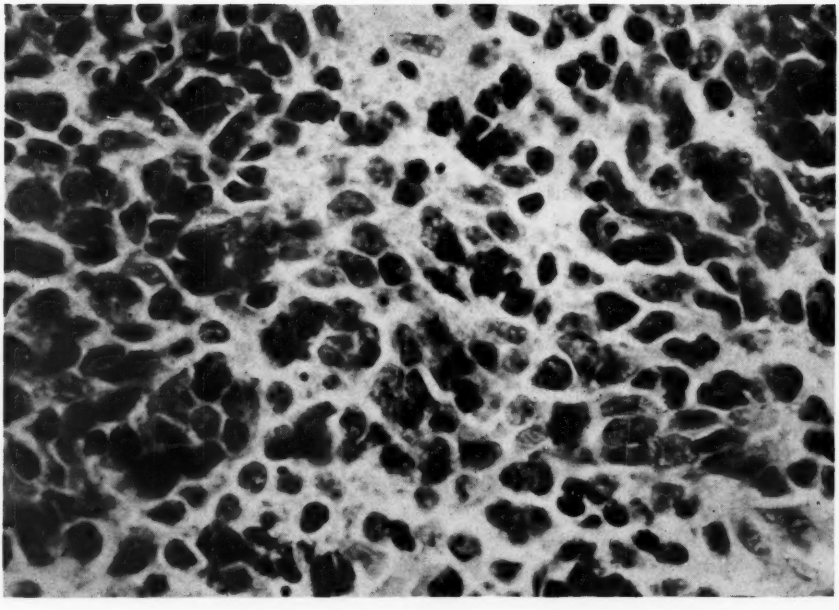
TABLE II. PATHOLOGIC FEATURES OF CARCINOMA OF THE LUNG EXPLORED BUT NOT RESECTED

Structures invaded by tumor		
Hilar and mediastinal nodes		16
Chest wall		12
Aorta		5
Heart		5
Trachea		2
Bronchoscopy		
Negative		20
Positive		19
Squamous without pearls	11	
Undifferentiated	4	
Outside report	2	
Basal	1	
Mixed form	1	
Surgical pathology		
Undifferentiated		16
Squamous without pearls		14
Mixed		4
Adenocarcinoma		2
Type of tumor with respect to location of biopsy		
Mediastinum		
Squamous without pearls		6
Undifferentiated		8
Mixed form		1
Adenocarcinoma		2
Chest wall		
Squamous without pearls		3
Undifferentiated		7
Adenocarcinoma		1
Mixed forms		3

There is some evidence to suggest that in this group the undifferentiated tumors tended to occur at a greater distance from the hilum. The one adenocarcinoma chiefly involved the mediastinum and the aorta, while of the mixed types, one spread mainly to the periphery and one was located chiefly at the hilum. The mixed forms (containing both squamous cells and adenocarcinoma) are worthy of comment in that they demonstrate that for really reliable diagnosis and study, large sections are indispensable. That different portions of the same tumor reveal strikingly different histologic patterns is well brought out by Phillips and co-workers.[2]

This nonresected group of cases demonstrate a somewhat different ratio among the commonly accepted classifications of adenocarcinoma, squamous carcinoma, and undifferentiated carcinoma. In this group there was but one adenocarcinoma. This is contrary to the usually reported frequency of adenocarcinoma which ordinarily comprises between one-third and one-fourth of all lung carcinomas. It will also be noted that keratinizing squamous tumors were absent. The majority of the tumors were either nonkeratinizing squamous or undifferentiated tumors.

A.

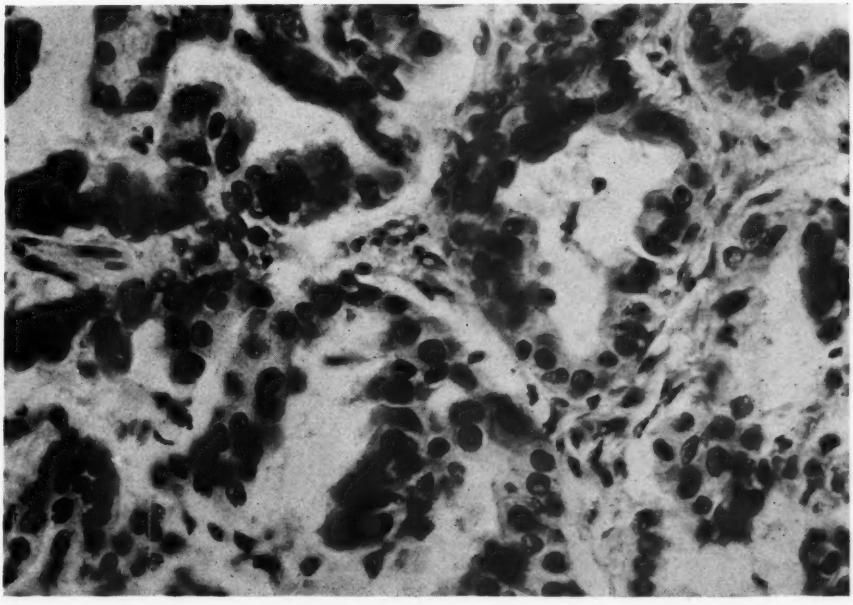


B.

Fig. 1.—*A*, Roentgenogram of a patient who had an undifferentiated carcinoma of the lung; *B*, microscopic appearance of this patient.

There were 36 autopsied but not explored patients with carcinoma of the lung. The average age of this group was 56 years, and 29 of the 36 were men. The correct diagnosis was made in one-half of the cases prior to autopsy. About

A.

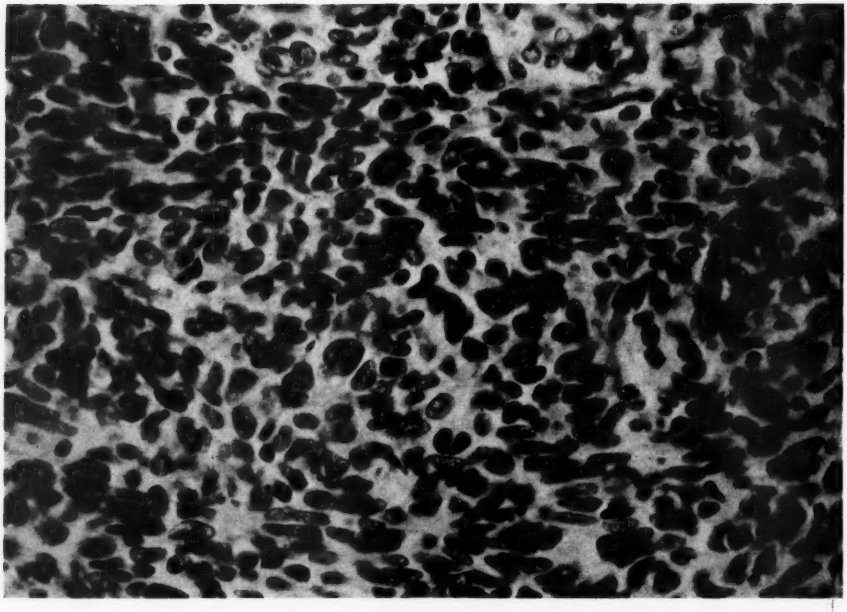


B.

Fig. 2.—X-ray therapy had been given without a proved diagnosis. *A*, X-ray appearance prior to death; *B*, microscopic appearance of the adenocarcinoma which arose in an old tuberculous scar.

the same ratio held true in Koletsky's series of 100, the correct diagnosis having been made ante-mortem in 56 of the cases. All of our 18 diagnosed cases were unsuitable for operation because of extensive pleural spread, or because of more

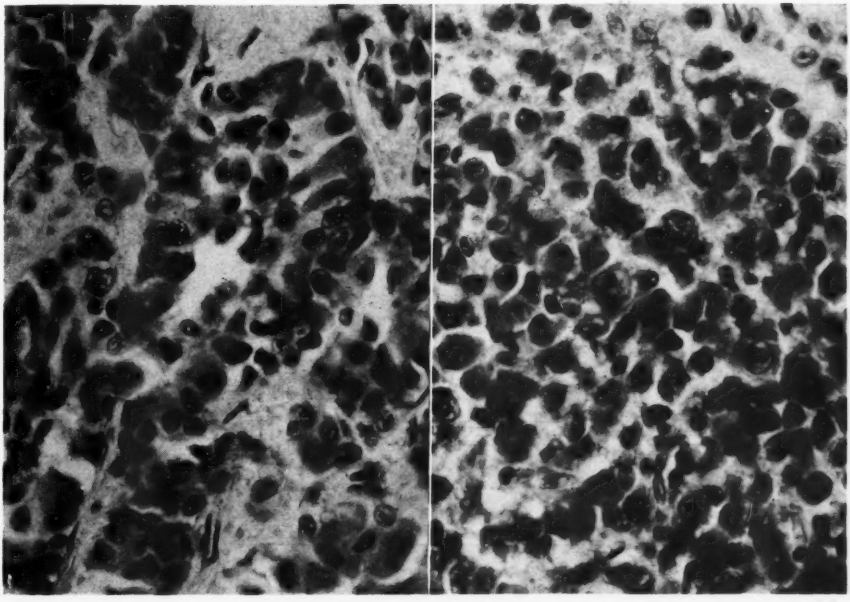
A.



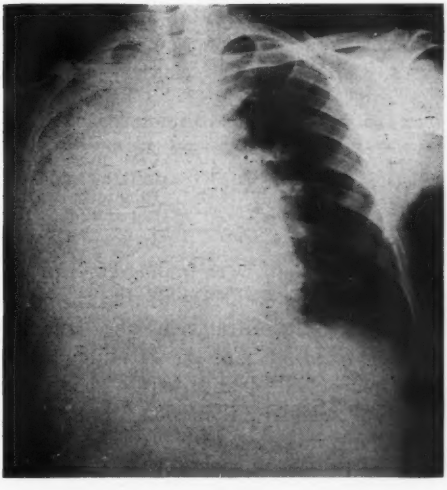
B.

Fig. 3.—*A*, Roentgenogram of an unexplored patient whose tumor area arose in the right main bronchus; *B*, microscopic appearance of undifferentiated tumor.

remote metastases. Briefly, the specific sites for spread of the tumor, in those correctly diagnosed, were: pleura, 10; chest wall, 5; the brain in 2, and the mandible in 1.



A. *B.*



C.

Fig. 4.—Shows two cell types in the same tumor. *A* is from the primary site, being an adenocarcinoma and *B* is an undifferentiated metastasis. *C*, X-ray appearance of the chest in the preceding case.

In the group of 18 diagnosed as primary lung tumors, the average age was 56 years, and 14 of the 18 were men. Nearly all of these patients had symptoms referable to the chest such as cough, chest pain, sputum, or dyspnea. Weight loss was also an important finding. The average duration of symptoms with respect to tumor histology was as follows: adenocarcinomas, eight months; squamous, four months; and the 1 mixed type had produced symptoms for 1 month.

Bronchoscopy was used in only 6 of these cases. In one, the examination was inconclusive. In 3, there was gross evidence of tumor, but no microscopic sections were made. Two of the 6 had microscopic sections; 1 of these showed squamous cells and the other was undifferentiated. The one which bronchoscopy reported as a squamous tumor really was undifferentiated according to the autopsy findings. The other case, that of D. H., had a bronchoscopic report of squamous-cell carcinoma of bronchus and was, at autopsy a squamous tumor.

Biopsies are frequently useful and may be obtained from various areas. Table III compares the result of biopsy in these cases with the autopsy findings.

TABLE III. A COMPARISON OF SURGICAL BIOPSIES WITH AUTOPSY DIAGNOSES TO INDICATE THE VARIABILITY OF THE CELL TYPE IN THE SAME PATIENT

CASE	SITE	BIOPSY REPORT	AUTOPSY REPORT
1	Cervical nodes	Squamous	Adenocarcinoma
2	Mandible	Squamous	Mixed
3	Larynx	Squamous	Squamous
4	Chest wall	Undifferentiated	Adenocarcinoma
5	Ilium	Undifferentiated	Undifferentiated

It is apparent that not too much confidence can be placed in the histologic report of the biopsied specimens. Many times, however, a careful physical examination will reveal nodes or lumps which can be biopsied. If positive for carcinoma, such information is helpful in establishing a diagnosis. The authors have obtained positive biopsies from such places as the posterior chest wall, axilla, lateral chest wall, skull, extremities, cervical nodes, and maxilla.

TABLE IV. THE LOBAR DISTRIBUTION OF THESE TUMORS WAS AS FOLLOWS

Right upper lobe	5	Left upper lobe	6
Right main bronchus	5	Left lower lobe	6
Right lower lobe	4	Undetermined	5
Middle lobe	2	Left main branches	3

Eighteen of the autopsy group were undiagnosed prior to death. Four of these were tiny incidental tumors occurring during the course of other diseases. Of the remaining 14, the clinical manifestations were caused by the bronchiogenic tumor, but were misinterpreted. Six of the 14 undiagnosed tumors were from autopsies on patients from outside institutions. The eight errors in diagnosis at this hospital consisted of mistaking the lesion for aneurysm, lymphoma, tuberculosis, lung abscess, and brain tumor. The histology of the undiagnosed group was as follows: undifferentiated 8, adenocarcinoma 7, and squamous 3. Four of this group were women. The average age of the 18 was 56 years. The lobar distribution of these tumors is seen in Table IV.

PATHOLOGY

Of the 36 autopsied carcinomas, 15 were adenocarcinoma, 14 were undifferentiated, 6 were squamous, and 1 was a combination of adenocarcinoma and nonkeratinizing squamous. The relationship between cell type, site of origin, and the tendency to either predominantly mediastinal invasion or widespread metastases is shown in Table V. It will be seen that in this rather small group the squamous variety tended to occur nearer the hilum whereas the more peripheral group was largely adenocarcinomas or undifferentiated tumors. There is a tendency in this group for the peripherally located undifferentiated tumors and for the adenocarcinomas to metastasize widely, whereas the centrally located squamous variety tend to invade locally and have a limited tendency to metastasize outside the chest. This impression conforms to previous reports by Koletsky[13] and Gebauer.[12]

TABLE V. THIRTY-SIX CARCINOMAS IN THE AUTOPSY FILE NOT OPERATED

		PERIPHERAL	CENTRAL	UNCERTAIN
Adenocarcinomas	15	9	4	2
Undifferentiated	14	6	7	1
Squamous	6	1	4	1
Mixed	1 (secondary bronchus)			
Widespread extrathoracic metastases in 18				
Adenocarcinoma		6	3	
Undifferentiated		5	3	
Squamous			1	
Extensive mediastinal spread in 11				
Adenocarcinoma		2	1	
Undifferentiated		2	2	
Squamous		1	3	

Some of the microscopic features may be discussed. There were three chief groups, as indicated above, adenocarcinoma, squamous-cell carcinoma, and the undifferentiated. Occasionally, bizarre forms are seen and not infrequently tumors composed of both adenocarcinomas and nonkeratinizing squamous tumors are found. The histology of the adenocarcinomas consists of abnormal acinous formation by irregular large or small columnar cells. The individual cells vary in their degree of differentiations, but usually present no problem in recognition. Mucous production is not a constant feature.

The squamous tumors are composed of either the keratinizing or nonkeratinizing group. The former is readily recognized by the flat sheets of polygonal cells, and the tendency to pearl formation. Prickle-cell formations are sometimes recognizable. The nonkeratinizing group is made up of large sheets of polyhedral cells, at times showing prickle formation, and no tendency to acinous development.

The third large group is the undifferentiated or "oat-cell" tumor. These probably were mistaken in earlier days for sarcoma. The cells are spindle or oval shaped, growing often in bundles and having a somewhat sarcomatous appearance. Ochsner[5] has commented on the different types which the relatively undifferentiated tumors may assume. His recent article contained excellent illustrations of these forms. A smaller group makes up a list of bizarre tumors

containing the so-called adenoma, which we believe to be malignant. Phillips[2] emphasized that mixed forms having more than one cell type may occur in the same tumor. Representative slides along with the roentgenograms of some of the various tumors are shown in Fig. 1.

Of the 36 autopsied, but not explored, lung carcinomas, 15 were adenocarcinomas, 14 were undifferentiated, 6 were squamous, and 1 was a mixed form. Four of the 6 squamous carcinomas were keratinizing while 2 were nonkeratinizing. In these cases, the adenocarcinomas and the undifferentiated, or "oat-cell" tumors, tended to lie toward the periphery and spread not only to mediastinal structures, but also to distant organs via the blood stream. The squamous variety tended to occupy a more central location and spread chiefly through adjacent mediastinal structures.

SUMMARY

The pathologic type and the clinical behavior of explored but nonresected lung carcinomas, and the lung carcinomas which came to autopsy without exploration have been compared with a group of resected tumors of the lung. It is our impression that such a study sheds some light on the behavior of these tumors. We feel that there is some correlation of cell types with clinical course. Of course, any far-advanced tumor will be inoperable. The tumors which appear to be less amenable to surgical therapy are largely the poorly differentiated ones and the adenocarcinomas. This impression is derived from the fact that the autopsied and the explored but not resected tumors were composed of 30 undifferentiated tumors, 17 adenocarcinomas, 16 nonkeratinizing squamous, 4 keratinizing squamous, and 5 mixed forms containing more than one all type. In contrast to this, Phillips and associates[2] found that all of their resected tumors were squamous cell in part or entirety.

REFERENCES

1. Lindskog, G. E.: Ann. Surg. **124:** 667, 1946 (Discussion).
2. Phillips, F., Basinger, Clair, and Adams, W. E.: J. THORACIC SURG. **19:** 680, 1950.
3. Adler, Isaac: Primary Malignant Growth of Lungs and Bronchi, London, 1912, Longmans, Green & Co.
4. Ewing, James: Neoplastic Diseases, ed. 4, Philadelphia, 1942, W. B. Saunders Company.
5. Ochsner, Alton, and associates: J. THORACIC SURG. **17:** 573, 1948.
6. Bloch, R. G., and Tucker, W. B.: Am. Rev. Tuberc. **50:** 405, 1944.
7. Adams, W. E.: Clinics **4:** 1035-1054, 1945.
8. Boyd, William: Canad. M. A. J. **23:** 210, 1930.
9. Fried, B. M.: Bronchiogenic Carcinoma, Baltimore, 1932, Williams & Wilkins Company.
10. Karsner, Howard: Human Pathology, ed. 6, Philadelphia, 1943, J. B. Lippincott Company.
11. Weller, C.: Arch. Path. **7:** 478, 1929.
12. Gebauer, P. W.: J. THORACIC SURG. **10:** 373, 1941.
13. Koletsky, S.: Arch. Int. Med. **62:** 636, 1938.
14. Adams, R.: J. THORACIC SURG. **17:** 306, 1948.
15. Neuhof, H., and Aufses, A. H.: J. THORACIC SURG. **17:** 297, 1948.

64.

THE MANAGEMENT OF CHYLOTHORAX

RICHARD H. MEADE, JR., M.D., GRAND RAPIDS, MICH., JEROME R. HEAD, M.D., CHICAGO, ILL., AND (BY INVITATION) CHESTER W. MOEN, M.D., BOSTON, MASS.

THE management of chylothorax was mainly a subject of academic interest until Lampson,[5] in 1946, demonstrated that the condition could be cured by ligation of the thoracic duct in the lower chest. Prior to this, only fifty-eight cases of traumatic chylothorax had been reported, and fewer reports of chylothorax due to other causes had appeared in the literature. According to Zesas,[12] the first description of a case of traumatic chylothorax was made by Bartolet in 1633. As about one-half of the cases of chylothorax have been associated with fatal diseases, and as they are rare, there has been little enthusiasm for working out a satisfactory method of treatment. However, the other one-half of the cases of chylothorax are caused by direct or indirect violence, or by injury during an intrathoracic operation. That it may occur following seemingly trivial trauma has also been known for a long time. The mortality from chylothorax, from all causes, has been put at 50 per cent by many writers. Recently such excellent presentations of the subject have been published by Lampson,[5] by Baldridge and Lewis,[1] and by Hodge and Bridges,[4] that any further survey of the whole subject would be superfluous. However, it is worth while to discuss further the subject of treatment, and to present three new cases in which different forms of treatment were successfully used.

Soon after Lampson submitted his article on traumatic chylothorax cured by ligation of the thoracic duct for the 1947 program of The American Association for Thoracic Surgery, we were asked to see a patient with chylothorax. She was 24 years of age, and had fallen down cellar steps, without apparent injury, three months before developing symptoms of pleural effusion. After nine weeks of study for a possible cause for chylothorax, which included a test of x-ray therapy, it was decided that it was due to the fall. Protein balance was maintained by means of a high protein diet and repeated infusions of plasma, and the pleural cavity was frequently emptied of its chyle. She was operated upon, and the thoracic duct was ligated just above the diaphragm. Although the approach to the duct was not as easy as described by Lampson, prompt recovery made this method of treatment seem to be the logical one (Figs. 1, 2, and 3). A short while after this patient was discharged from the hospital another patient, a woman 58 years of age, with chylothorax, was referred to us. After another exhaustive study to rule out a suspected malignancy, and after repeated aspirations of the chyle and partial replacement of the lost protein by plasma infusions, she was operated upon. At this operation a section of the thoracic duct was supposedly resected a short distance above the diaphragm on the right, but on histologic examination it was seen to be splanchnic nerve.

Read at the Twenty-ninth Annual Meeting of The American Association for Thoracic Surgery, New Orleans, La., March 29-31, 1949.

Fig. 1. Fig. 2. Fig. 3.

Fig. 1 (Case 1).—Chest roentgenogram taken on admission to the hospital showing massive left chylothorax.

Fig. 2 (Case 1).—Chest roentgenogram taken after almost complete replacement of the chyle by air shows marked collapse of the left lung but no evidence of other abnormality.

Fig. 3 (Case 1).—Chest roentgenogram taken eleven weeks after the ligation of the thoracic duct and the lung fully re-expanded except for the extreme apex.

With this information, and with the appearance of chyle in the opposite pleural cavity, she was operated upon again in an effort to ligate the leaking duct. In the history it had been learned that she had fallen down some steps six months previously without apparently being hurt. Because of our first case we thought that this fall was the etiological factor in this case. At the first operation nothing abnormal could be found except the chyle in the pleural cavity. The second operation was done through the same right side because it was thought that the leak was on this side but that the chyle had not been able to re-enter this pleural cavity as a result of its obliteration by postoperative adherence of the pleural surfaces. Closed drainage of the right pleural cavity had been maintained for two days after the operation. At the second operation it was seen that all of the pleural space had been obliterated by the re-expanded lung. An eggnog had been given to the patient two hours before the operation in order to make the thoracic duct more prominent. After an exhaustive search, chyle was seen leaking from a small duct. This vessel was ligated, but it was obviously not the only channel through which the chyle was flowing. After further search failed to reveal another duct, the space between the vertebral column and the diaphragm was packed with Oxycel gauze in hope of blocking any other pathway. The chest was closed with the usual provision for closed drainage. Re-expansion of the lung again occurred promptly but chyle reappeared in the left pleural cavity. This chyle was aspirated at frequent intervals without any effect on its rate of formation. Accordingly, closed drainage of the left pleural cavity was established, and within seven days there was no further leakage of chyle. She was discharged from the hospital, and for three months got along well. She then developed a severe and extensive dermatitis, which failed to respond to treatment at home so that she was readmitted to the hospital. The last roentgenogram of the chest had shown a shadow in the region of the fissure between the middle and lower lobes and it was thought that she might have some fluid in connection with the disease causing the dermatitis. Two days after entering the hospital she developed jaundice and died within twelve hours of a fulminating hepatitis. At autopsy a prolonged search failed to reveal any trace of a thoracic duct. There was a small amount of chyle in each pleural cavity and in the pericardium. An extensive flat growth of tissue was found in the retroperitoneal space and in the posterior mediastinum. This proved to be lymphosarcoma and was found to involve the lungs, the liver, and many other parts of the body. It was considered to be the cause of the chylothorax. The hepatitis was thought to be due to the large quantity of plasma which she had received four months previously (Figs. 4, 5, 6, and 7).

A third case of chylothorax was seen the next year. This patient was 54 years of age. He was known to have an extensive lymphosarcoma involving the mediastinum and apparently causing the chylothorax. At first, he was treated by repeated aspirations of the chyle but these were of no avail and closed suction drainage was then established. The lung re-expanded and the chyle stopped accumulating. He continued the downhill course and died as a result of the lymphosarcoma.

Fig. 4. Fig. 5.

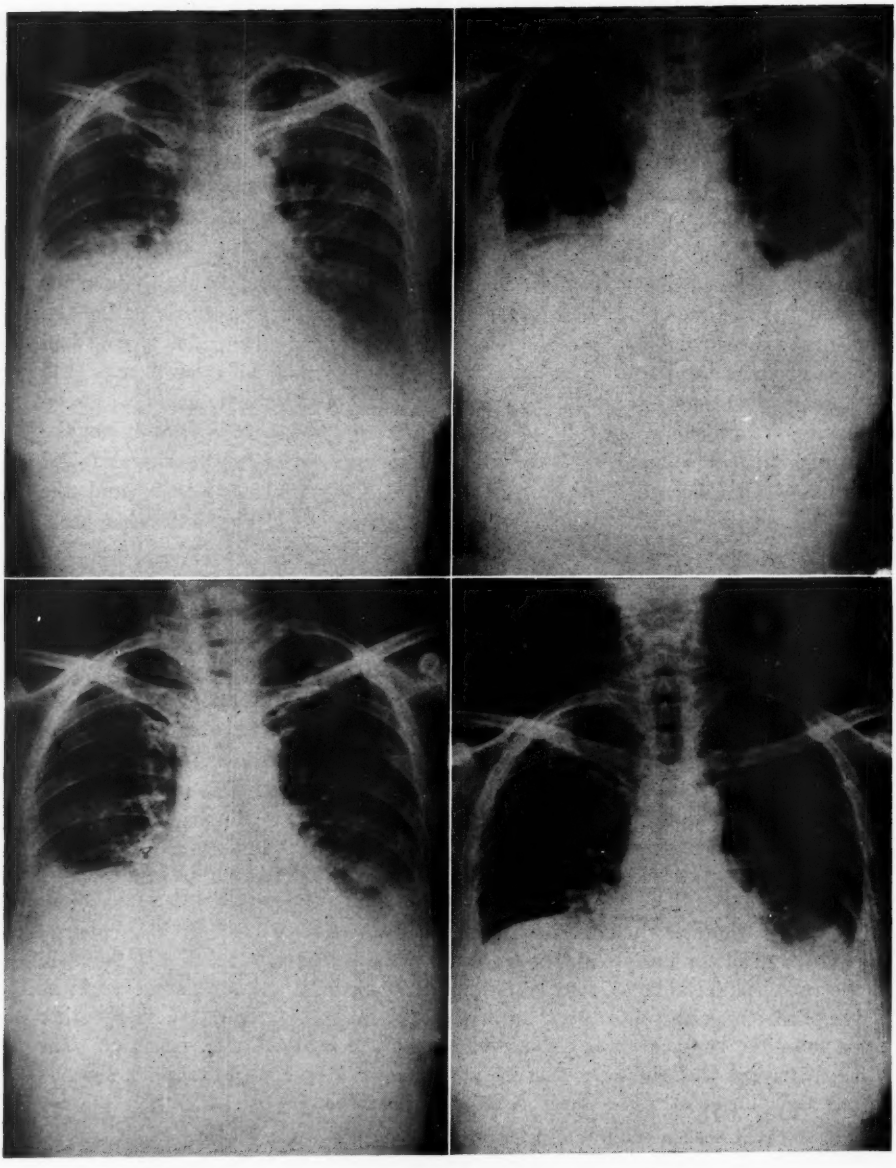


Fig. 6. Fig. 7.

Fig. 4 (Case 2).—Chest roentgenogram taken on admission to the hospital showing evidence of small amount of fluid in both pleural cavities.

Fig. 5 (Case 2).—Chest roentgenogram taken five days after the first operation through the right pleural cavity, showing evidence of chyle in the left pleural cavity.

Fig. 6 (Case 2).—Chest roentgenogram taken forty-two days after second operation on the right and seven days after starting closed drainage of left pleural cavity.

Fig. 7 (Case 2).—Chest roentgenogram taken five weeks after cessation of leakage of chyle shows evidence of slight pleural change.

These three cases illustrate a number of important points with which one is concerned in the management of patients with chylothorax. Before discussing the details of management it is important to review some of the facts known about pathogenesis, blood picture changes, the effects of chyle on the pleura, the problem of replacement of the important food elements in the chyle, and the anatomy of the thoracic duct.

A great many causes for chylothorax have been recorded and suggested. These will not be reviewed here. Most of them are obvious and need no comment. In our three cases there were apparently two main etiological agents. In the first case the only possible factor was the fall down the steps three months before the onset of symptoms of pleural effusion. The fall had been so slight that the patient did not remember it until she was made to review all possible injuries which might have caused a rupture of the thoracic duct. Operation revealed that the chyle had infiltrated the mediastinum and the root of the lung, and that it had escaped into the left pleural cavity through a small fistula in the mediastinal pleura just below the inferior limit of the pulmonary ligament. This finding seemed to fit in well with the long interval between the injury and the onset of symptoms. The duct was bound down in the surrounding tissues, but this was thought to be due to the reaction to the extravasated chyle. However, had there been some inflammatory process in this area before the fall, which had fixed the duct to the underlying vertebrae, it can be more readily conceived that a sudden hyperextension could have ruptured the duct. Sudden hyperextension of the spine has been considered a probable cause. It is well known that rupture of the gut, or of the aorta, usually occurs by tearing close to the junction between a movable and a fixed segment of the tube. It would seem to us, therefore, that unusual fixation of the duct to the surface of the vertebrae by inflammation, or by congenital bands, would be necessary before any movement of the spine could rupture a vessel so freely movable and so elastic as the normal thoracic duct. The state of distension of the duct must contribute to its vulnerability. In his case, Lampson[5] attributed the rupture to a sudden, severe increase in intraductal pressure caused by a coughing spell. Other similarly slight disturbances have been considered to have caused chylothorax.

In our second patient, until the autopsy, we thought that the cause of the chylothorax was the same as in our first case. When the autopsy showed the presence of chyle in both pleural cavities, and in the pericardium, and also a diffuse lymphosarcoma involving the mediastinum and retroperitoneal tissues, it seemed obvious that the fall could only have played a part in the production of the original chylothorax. Since, at and after each operation in our case, a study of the tissue from the region of the thoracic duct failed to show any evidence of lymphoma, it is hard to believe that the tumor could have been the sole cause for the chylothorax. It seems that the channels through which the chyle passed were fine ducts, and that one or more of them had become fixed to the surface of the vertebrae by changes in the tissue preceding the development of the lymphosarcoma. This fixation would then have made them more vulnerable to rupture from hyperextension of the spine

when she fell down the steps. The delay in the appearance of symptoms could be explained as in the first case, only that in this one there was no extensive infiltration of the mediastinum, and no outlet through the pleura was seen.

In the third patient there was no operation and no autopsy. The patient was known to have an extensive lymphosarcoma involving the mediastinum. The clinical and roentgenographic findings were characteristic and these had been substantiated by biopsy of a cervical lymph gland. It has frequently been mentioned in the literature that chylothorax develops as a result of blockage of the thoracic duct by tumor or by enlarged lymph glands. That such blockage can produce chylothorax seems unlikely in view of the experimental work of Blalock and associates,[2] who had no success in producing chylothorax in dogs by blocking all available thoracic ducts. It would seem that it would be necessary for the tumor actually to invade the duct, or to fix it so that it could later be ruptured by some sudden movement of the spine, or by sudden increase in intraductal pressure.

Experimentally and clinically, it has been noted that following the rupture or ligation of the thoracic duct there is a striking drop in number, or complete disappearance, of the lymphocytes and eosinophils in the circulating blood. As the lymphocytes are known to be carried through the thoracic duct to the blood stream, it is not remarkable that there should be an effect on their numbers by disturbances of the duct. Why the eosinophils are effected is not known, but their disappearance is of little diagnostic importance since they are usually present in such small numbers that their absence would not be noted. The marked drop in the lymphocyte count can be of great diagnostic value, especially in accident cases when there is a chest injury but no evidence of injury to the thoracic duct. If there is need for thoracic exploration in such a case, and the lymphocytes are markedly decreased in number, a search should be made for free chyle, and the thoracic duct ligated if chyle is found. In our first case the lymphocytes had dropped from 3,744 per c.mm. on admission to the hospital, to 540 six days before operation. Four days after operation there were no lymphocytes in the blood. Eight days later there were 386 per c.mm. and just before her discharge from the hospital eleven days later, there were 1,443. Within the next month the blood picture had returned to normal. In the other two patients the lymphocytes were at a low level during the time the chylothorax was present, but the changes were not as striking as in the case in which the duct was tied.

The local effect of chyle on the pleura is of importance when the leakage is not promptly stopped. It causes an inflammatory reaction which results in thickening of the pleura with a loss in its elasticity and the deposition on its surface of a layer of exudate. Fibrin may be precipitated in masses of varying size and add to the thickness of the coating on the lung. In our first patient, who was not operated on until nine weeks after the discovery of her chylothorax, the lung was collapsed and could not be expanded at all until a tedious decortication had been completed. There was no well-defined "peel" as found in chronic hemothorax or in most cases of chronic empyema. It was necessary to remove a considerable amount of the true visceral pleura. The

infiltration of the root of the lung with the chyle made it impossible to secure full re-expansion of the lung at the time of the operation. Full re-expansion of the lower two-thirds of the lung occurred in a few days after the operation with the aid of closed drainage. The apex did not fully re-expand for another two months. This caused no symptoms and she was discharged from the hospital three weeks after the operation. The importance of keeping the lung expanded by frequent aspiration of the chyle is obvious, but, as in our case, it may be impossible. The failure to keep the lung expanded is further reason for speed in stopping the leak of the chyle.

Death from chylothorax, unless the condition is unrecognized and allowed to cause asphyxia, is due to the progressive loss of the fluid, protein, and fat. As chyle is bacteriostatic, we know of no instances in which infection of the chyle has caused death. Before it was demonstrated that the escape of the chyle could be stopped by operation or by closed drainage of the pleural cavity, the importance of replacement of the protein and fat lost in the chyle was great. It is still an important problem. The idea of returning the chyle to the blood stream after its aspiration from the pleural cavity was an obvious one since it is a fluid that normally flows into the blood stream, and it apparently undergoes little change while standing in the pleural cavity. Since this procedure was first reported by Oeken,[7] in 1908, it has been used in a number of instances with varying results. Its use without mishap by Little, Harrison, and Blalock,[6] in which they returned 22 liters of chyle to a patient, was reported in 1942. Others have reported the same results but there have been reports of sudden death following this procedure in two patients. The one reported by Whitcomb and Scoville[11] came on suddenly after the slow infusion of a small amount of refrigerated, citrated chyle. It was anaphylactic in character. In the other case, reported by Peet and Campbell,[8] death was sudden in occurrence and no cause for it could be found. It was suggested by Whitcomb and Scoville[11] that the patients who are to receive infusions of chyle should first be skin tested with the chyle to determine a possible sensitivity. This seems unnecessary, as one could hardly be sensitive to a natural body fluid which under normal conditions is constantly flowing into the blood stream. These authors also suggest that the fat droplets in the chyle be measured, and if found to be of greater diameter than 3 micra, the chyle should not be used. If coalescence of the droplets can occur in either the pleural cavity, or outside, this would seem to be a wise precaution. In view of the successful, repeated intravenous infusions of freshly aspirated chyle in the case reported by Little, Harrison, and Blalock,[6] this method would seem to be the best and the least likely to give rise to trouble. However, in some cases there will be precipitation of fibrin, and the fibrin may form large masses. The injection of such fluid into the blood stream could certainly cause disturbances. Therefore, it would seem preferable to administer the chyle after filtration, but as soon as possible after aspiration. It is our belief that, until further experimental work has been done on the causes of reaction following the infusion of chyle, it should not be used.

It seems much wiser to prevent depletion than to combat it. A high protein diet and intravenous infusions of amino acids, and an occasional blood transfusion may be used temporarily. Plasma should not be used. It may, as it did in our second case, produce a fatal hepatitis. To prevent malnutrition and to forestall a thickened pleura and permanent collapse of the lung, closed suction drainage or ligation of the thoracic duct should be undertaken early if aspiration is ineffectual.

The thoracic duct is not always the single, well-defined structure that is pictured in standard anatomic works. This was forcibly drawn to our attention during the course of the two operations on our second patient. It always enters the chest through the aortic hiatus of the diaphragm and almost invariably ascends between the azygos vein and the aorta, on the anterior surface of the vertebrae. However, there are variations. Stuart,[9] in 1907, reported that in his dissections the variations were more frequent than the supposed normal arrangement and that the statement that the thoracic duct was a single channel throughout the chest was misleading. Davis,[3] in 1915, described nine types of thoracic duct found in dissecting twenty-two cadavers. However, more recent studies do not confirm these earlier ones. Baldridge and Lewis,[1] in a study of twenty bodies, found a single thoracic duct in each. Van Pernis,[10] in careful studies of 1,081 bodies at autopsy, found a great uniformity except in the small branches of the upper portion. One of us (C. W. M.), working in the department of anatomy at Northwestern University Medical School, studied the thoracic duct arrangement in 135 cadavers. In 78 per cent there was a single duct. In 17 per cent there was a short, single duct which divided into two, which united either below or above the diaphragm. In 5 per cent there was a single duct which divided into two and which ran through the chest. From all of these studies it is apparent that the chance of encountering real difficulty in finding the thoracic duct in the lowest part of the chest should be extremely rare (Figs. 8 and 9).

Having considered the various factors involved in chylothorax, a definite plan for the management of such cases can now be outlined. As it is known that one-half of the recorded cases of chylothorax have recovered after simple aspiration of the chyle, with or without replacement of the chyle, it would be wrong to advocate a more radical measure as the first form of treatment. Except in those cases in which chest exploration must be done for the control of an associated lesion, the immediate ligation of the thoracic duct should not be considered. First, aspiration of the chest should be used at frequent intervals. This should be continued if there is evidence of decrease in the amount of chyle leakage. If not, closed drainage should be started within ten days to two weeks. Whether or not there should be definite suction applied would seem to depend on the ease with which the fluid is removed. In our first case, in which closed drainage was used, there was no suction. In the second one there was, not because of any special indication, but because the operator considered this to be the quicker method of accomplishing the desired result. If suction drainage fails to bring about re-expansion of the lung, and cessation of the chyle leakage, then operation must be done. No

longer than two weeks should be allowed for this second stage of treatment since the danger of encapsulation of the collapsed lung is real. When operation is decided upon we feel that the object should be simple ligation of the duct at its lowest accessible point, with resection of a small segment for histologic verification of the structure, and for determination of any pathologic processes in the duct. There is no evidence, of which we are aware, that simple

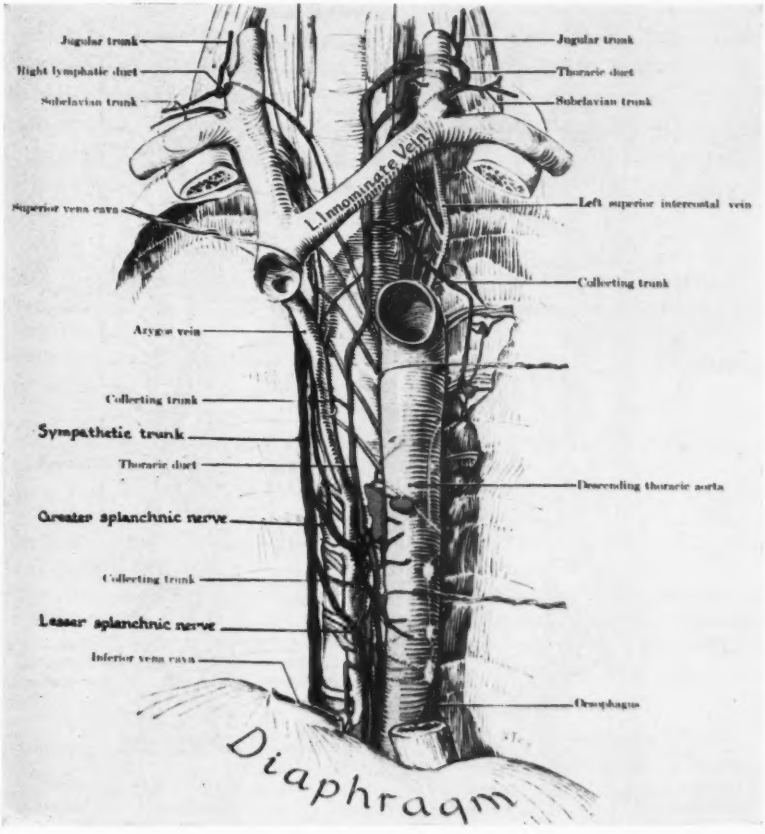


Fig. 8.—Typical course of the thoracic duct in the chest. The close proximity of the right splanchnic nerves to the duct is well shown. (Modified from Fig. 319, in "An Atlas of Anatomy" by J. O. Boileau Grant, Baltimore, 1943, Williams & Wilkins Company.)

ligation of the duct is not sufficient to stop permanently the flow of chyle. The leakage of chyle from the duct after the closure of its divided ends by silver clips, reported by Whitcomb and Scoville,[11] is no condemnation of ligation of the duct, but only of this method of closure. Hodge and Bridges[4] have recently advocated the anastomosis of the severed thoracic duct and the azygos vein, because they feel that simple ligation may be followed by recanalization of the duct, and further leakage. We do not believe there is

any real evidence for this, and although we admit the theoretical excellence of their proposal, and congratulate them on their successful accomplishment in a human case, we feel that it is a needless and difficult procedure.

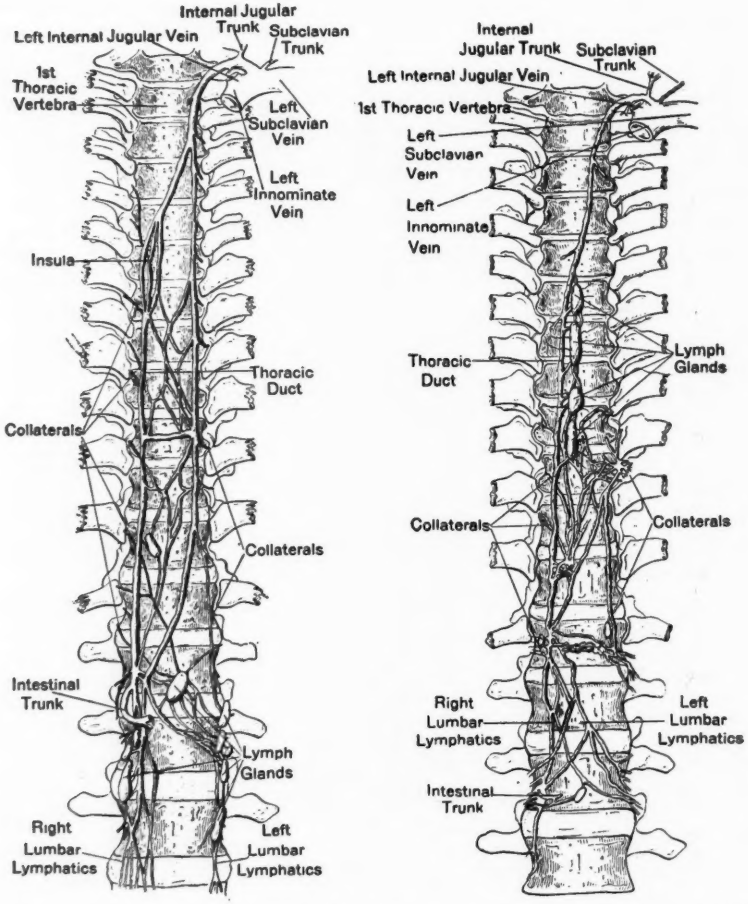


Fig. 9.—Unusual types of thoracic duct. The one on the right probably resembles the arrangement of the ducts in our second case. (Taken from illustration of dissection by H. K. Davis, in "Thoracic Surgery," by Howard Lilienthal, Philadelphia, 1925, W. B. Saunders Company, which was published in that volume through the courtesy of H. K. Davis, from the American Journal of Anatomy, January, 1915.)

SUMMARY AND CONCLUSIONS

Three cases of chylothorax due to different causes, treated by different methods, were successfully controlled. In one, due to a fall producing no outward evidence of injury, the thoracic duct was successfully ligated low in the chest. In the second, in which a similar fall seemed to play a role, two unsuccess-

ful attempts to find the thoracic duct was followed by closed drainage, and cessation of the leakage of chyle. Death, three months later from a fulminating hepatitis, was followed by an autopsy revealing no recognizable thoracic duct, but small amounts of chyle in the pericardium and both pleural cavities, and a flat, lymphosarcomatous growth in the retroperitoneal and posterior mediastinal spaces. The third patient's chylothorax was due to a widespread lymphosarcoma. Suction drainage controlled the chylothorax but the patient died of the disease. In the treatment of patients with chylothorax, unless operation is needed for an associated thoracic lesion, ligation of the duct should be used only after the simpler methods of treatment by aspiration of the chyle and by closed drainage have failed. Replacement of protein lost in the chyle should be by high protein diet and intravenous administration of amino acids, until further experimental work has been done on the cause of reactions following the intravenous administration of the aspirated chyle.

Acknowledgment.—The authors wish to acknowledge their indebtedness to Dr. Paul Rhoads, Dr. Gilbert Marquardt, and Dr. Henry Wilson for giving them the opportunity to manage the patients. To Dr. T. C. Laipply we owe thanks for the laboratory studies and to Dr. Henry Wilson for his careful studies of the blood in our second case. To Dr. Barry Anson we are grateful for making possible the anatomic studies.

ADDENDUM

Since the presentation of this paper two other cases of chylothorax have been seen by one of us (R. H. M.), in each of which recovery promptly followed closed drainage of the pleural cavity. The first patient was a woman 35 years of age who developed symptoms four days after back diving, an unusual form of exercise for her. She had roentgen-ray evidence of wedging of the fourth dorsal vertebra which was not associated with any remembered accident. It was thought that the rupture of the duct had resulted from the sudden hyperextension of the back with the thoracic duct fixed in the region of the wedged vertebra. The second patient was a young woman who was seen at the Boston City Hospital. Chylothorax had developed while she was a patient undergoing studies for an obscure heart condition, and no etiological factor could be found. She was successfully treated by Dr. John Strieder.

REFERENCES

1. Baldridge, Robert R., and Lewis, Robert V.: Traumatic Chylothorax: A Review of the Literature and Report of a Case Treated by Ligation of the Thoracic Duct and Cysterna Chyli, Ann. Surg. **128**: 1056, 1948.
2. Blalock, A., Cunningham, R. S., and Robinson, C. S.: Experimental Production of Chylothorax by Occlusion of the Superior Vena Cava, Ann. Surg. **104**: 359, 1936.
3. Davis, H. K.: A Statistical Study of the Thoracic Duct in Man, Am. J. Anat. **17**: 211, 1915.
4. Hodge, G. B., and Bridges, Hunter: Surgical Management of Thoracic Duct Injuries, Surgery **24**: 805, 1948.
5. Lampson, R. Starr: Traumatic Chylothorax; a Review of the Literature and Report of a Case Treated by Mediastinal Ligation of the Thoracic Duct, J. THORACIC SURG. **17**: 778, 1948.
6. Little, J. M., Harrison, C., and Blalock, A.: Chylothorax and Chyloperitoneum, Surgery **11**: 392, 1942.
7. Oeken: Ein Fall vonZerreissung des Ductus Thoracicus infolge Brustquetschung, München med. Wchnschr. **55**: 1182, 1908.
8. Peet, M. M., and Campbell, K. N.: Massive Chylothorax Following Splanchnicectomy, Univ. Hosp. Bull., Ann Arbor **9**: 2, 1943.
9. Stuart, W. J.: Operative Injuries of the Thoracic Duct in the Neck, Edinburgh M. J. **22**: 301, 1907.

10. Van Pernis, Paul A.: Personal communication.
11. Whitcomb, B. B., and Scoville, W. B.: Postoperative Chylothorax, Arch. Surg. **45**: 747, 1942.
12. Zesas, D. G.: Die nicht operative enstanden Verletzungen des Ductus Thoracicus, Deutsche Ztschr. f. Chir. **115**: 49, 1912.

DISCUSSION

DR. J. GORDON SCANNELL, Boston.—A recent case of intractable chylothorax which we had at Massachusetts General Hospital may be apropos of Dr. Meade's excellent review of this subject. Unfortunately, our combined efforts were not attended by the same success which he has had.

The patient was a 26-year-old man whose initial complaint was elephantiasis, but who, shortly after admission, was shown to have a right chylothorax and a chylous pericardial effusion. The former failed to subside with repeated aspirations. There was no history of trauma, nor were we able to establish a diagnosis of either tuberculosis or tumor. It was of great interest, however, that his half-brother had died at the same age, 26 years, of a chylous ascites associated with elephantiasis with dependent edema. In the course of hospitalization, massive amounts of chyle were removed from the chest without improvement (slides). Exploration was therefore advised and carried out. At the time of this first exploration his condition on the table was very poor, but the operator, Dr. Soutter, was able to ligate the thoracic duct at about the level of the ninth dorsal vertebrae as well as drain the pericardium into the right pleural cavity. There was no evidence of a primary cause of the disease and his condition on the table precluded further search. Immediately following this procedure, he did remarkably well so far as general cardiovascular state was concerned; but the accumulation of chyle continued, in fact rather increased, now in both pleural cavities. In the course of the next six weeks he became a serious nutritional problem—as Dr. Meade has indicated is likely to happen—and we felt that another attempt to stop the leak, without knowing where the leak was, was in order. Our thought was that possibly we could prevent the flow of chyle by resection of the duct or the cisterna chyli below the diaphragm with obliteration of the tract by suture. Therefore, he was re-explored through the right chest and an operative sketch of the procedure is shown (slide). In this case the right tenth rib was resected; the lower thoracic duct was picked up lying between the aorta and the azygos vein and followed down through the diaphragm by dividing the right crus of the diaphragm completely. The upper one-half of the cisterna was resected, all entering branches ligated, and the bed of the duct obliterated. For a matter of two weeks the patient accumulated very little chyle in the chest, but then reverted to the former condiion. He subsequently died about six weeks later. At autopsy he had a queer type of fibrosis involving the lymphatics of the lower extremities and a generalized fibrosis of the retroperitoneal and retropleural spaces. In view of the generalized condition of the lymphatic system, it is not surprising that the specific surgical attack on one of the collecting systems failed to arrest the course of the disease.

As an addendum, I might mention that in studying this patient, it was Dr. Churchill's suggestion that we might try to visualize the thoracic duct in the animal and possibly in the patient with radiopaque dye. This was done in a dog. The animal was explored through a left lumbar incision and a small polyethylene tube was put in the cisterna chyli which was distended by a previously eaten fat meal. The end of the tube was brought out to a little capsule beneath the skin. The following day 10 c.c. of 35 per cent Diodrast were injected into the capsule and excellent x-ray visualization of the thoracic duct was obtained (slide). This was repeated one week later and showed no gross damage to the duct. Two weeks later we were able to aspirate chyle from this sampling system.

DR. F. R. HARPER, Denver.—I should like to add one case to this splendid report of Dr. Meade's and the other discussors. The patient was a 42-year-old man who had bilateral chylothorax with collection of tremendous amounts of chyle. We carried on with aspiration for about two months, after which time the chyle was forming so rapidly that it was necessary to aspirate as much as 1,400 c.c. on each side every second day in order to allow the patient

to breathe freely. The patient's nutrition was going down very fast. For the preceding reasons an exploration was done, as has been shown by Dr. Meade, through the right side of the chest. We identified the structures in the region, namely, the azygous vein, the sympathetics, and the aorta, expecting to find some difficulty in identifying the thoracic duct. However, in the region where the thoracic duct should be there was a structure about as big as my index finger. In following this structure we found that it thinned down to the size of the normal thoracic duct, just below the hilus. I sent a specimen for frozen section. It was reported as being inflammatory. The report was erroneous, however, because it subsequently proved to be Hodgkins' disease. However, on the basis that it was inflammatory, I resected the thoracic duct and opened the diaphragm and resected part of the cisterna chyli. There was some leaking of the lymph vessels, the collaterals were picked up and ligated as well as possible, then some Gelfoam was placed where the duct had been resected. The chest was drained, by under water seal drainage, there was very little chyle from the right side of the chest. The left side had to be aspirated twice, then the chyle stopped forming. The patient's nutrition was very poor for the first ten days but, following that, he picked up and gained in weight and is feeling very well at the present time. It is about three and one-half months since the operation.

This case it seems to me brings out two points; the thoracic duct can be resected successfully in the right lower chest. In bilateral chylothorax, if the approach is made on the right side, ligating the thoracic duct at its origin will stop formation of chyle on the left side.

DR. WILLIAM R. RUMEL, Salt Lake City.—I would like to present another case of traumatic chylothorax which was treated successfully by surgery. In evaluating the results of surgical treatment it is very important to differentiate between cases of true traumatic chylothorax and the cases mentioned by Dr. Harper and Dr. Meade, where there is other serious associated disease. It seems to me that the problem in the two types is entirely different.

This case concerned a 5-year-old white boy who was playing with a pocket knife on July 9, 1947. He fell forward in such a manner that the 2¼ inch blade entered the base of the neck just above the inner end of the left clavicle approximately between the two heads of the sternocleidomastoid muscle. There was very little bleeding and after the mother applied an antiseptic dressing he continued to play. For four days he was asymptomatic but at that time developed a dry hacking cough and dyspnea. The family physician found evidence of a left hydrothorax. The symptoms were relieved by thoracentesis for another five days. At this time thoracentesis had to be repeated, with removal of 500 c.c. of milky fluid. Because of the appearance of the fluid he suspected the possibility of chylothorax and called me on the phone. I suggested that he send the child in for further treatment, little realizing that I was to find out in the next two or three days that the surgery which I had in mind was associated with 100 per cent mortality, according to the literature. Had I been a little better informed on the subject, I probably would have sent him to my nearest competitor. At any rate, he arrived at the hospital. He was moderately ill, with a temperature of 102° F., a pulse of about 160, and a respiratory rate of 40 with a moderate degree of dyspnea. Thoracentesis again revealed milky fluid which, on subsequent examination, was proved to be chyle.

He was placed on the generally recommended medical therapeutic regime for a period of twelve days during which time the condition deteriorated progressively; so that it was apparent that something further would have to be done. Operation was decided upon, although with a great deal of fear and trepidation, because during that time I was still unable to find a record of a single case that had been treated successfully by surgery. Somehow I overlooked the report of Dr. Ralph H. Loe from Seattle, who had reported a similar case a few months previously. On July 31, 1947, 22 days after the injury, and about one and one-half hours after administration of milk and cream, he was anesthetized and an approach made through the left supraclavicular area. I was delighted on finding the duct without difficulty, including some of its ramifications, and was able to follow it down for a distance of about two inches below the suprasternal notch. At this point it disappeared into a mass of scar tissue. It was possible to dissect down in front of and behind this tissue and while it

was not possible to actually demonstrate a tear in the duct, it was assumed that it communicated with the pleural space at this point. Two silk ligatures were placed around the area, one below the scar tissue and one above. These were tied firmly and the incision was closed. Fortunately he made a very uneventful recovery. It was not necessary to aspirate the chest even on one occasion. Since that time he has developed in a perfectly normal manner.

If we add this case to Dr. Meade's—that is, the one which was not associated with another serious underlying lesion—and include the cases reported by Loe, Peet and Campbell, Lampson, and Baldridge and Lewis, it will make a total of six cases of traumatic chylothorax treated surgically. In each case a successful result was obtained with the exception of that reported by Peet and Campbell where death occurred suddenly following intravenous administration of chyle, presumably due to anaphylaxis. In evaluating the risk of surgery in these cases it would seem proper to eliminate this death inasmuch as it apparently was due to the rather dangerous procedure of parenteral administration of chyle.

From this, it would appear to me that perhaps we could be even a little more aggressive than Dr. Meade suggests, and go right ahead with surgical treatment in these traumatic cases as long as we can show that the mortality rate is below that of the ordinary medical measures, that is, around 40 to 50 per cent, and as long as these patients obtain good results following surgery. It seems that the only objection to this recommendation would be continued acceptance of the statement that has been made repeatedly in the medical literature to the effect that any direct surgical attack on the thoracic duct is associated with 100 per cent mortality. If we look into the basis for this statement it will be found that it is based on several cases treated by various surgical procedures, in only one of which—that of Whitcomb and Scoville—the duct was actually ligated.

DR. R. G. KLEPSER, Washington, D. C.—I would like to add to this list one additional case of traumatic chylothorax successfully treated by ligation of the duct and also to suggest a method to make the diagnosis and the operation somewhat easier. We have at the present time two patients with chylothorax in the Naval Medical Center Hospital at Bethesda; one is a traumatic case upon whom I operated last Friday, six days ago. He is a 290 pound man who was in an auto accident in July, 1948. He had been treated as a cardiac case because of retrosternal pain for six months before fluoroscopy was done. A diagnosis of chylothorax was made after aspiration of the fluid. The fluid was repeatedly aspirated, about 1,000 c.c. being removed every other day; the chyle continued to leak into the right chest. During this time we came upon a method of diagnosis by feeding these patients fat which contained lipophilic coal-tar dyes. This is not new; Fletcher in England had given Sudan III to a patient who had chyle in the urine, and upon recovering the Sudan III in the urine made the diagnosis of chylouria in 1930.*

When these dyes, using Sudan III or other colored dyes, are ingested, the chyle, about one to two hours later, becomes colored. Only the fat is colored and by churning the chyle the fat pellicle can be removed; it can be colored red or green or blue or any color desired. The vegetables dyes are valueless. Oleomargarine dyes were used and were not reobtained in the chyle; the coal tar dyes, of which Sudan III is one, are the best. We used a green dye before operating, putting it in olive oil and giving it through a duodenal tube several hours prior to operation. When the chest is opened the ducts and the chyle are stained, making identification of the ducts much easier. The dye remains attached to the fat, and no other structures are stained. Because of contrast, a green dye seems preferable.

We ligated a large duct and three smaller branches. There was no cortex or peel over the lung in spite of the fact that this lung had been down from six to nine months before, and we had no trouble re-expanding the lung. The chest was closed without drainage. A roentgenogram was taken yesterday and shows no fluid in the chest. In this case the chylothorax was on the right side. Because the lower portion of the duct is so much more accessible, I believe the right-sided approach is preferable for duct ligation in a left chylo-

*Fletcher, H. Morley: Proc. Roy. Soc. Med., 1930.

thorax if preoperative thoracentesis shows the left lung to be re-expandible. Identification of all of the duct branches would be more certain and safer than attempting to immobilize the aorta to reach the duct from the left thorax.

DR. ARTHUR S. W. TOUROFF, New York.—I would like to add a report of two additional cases of traumatic chylothorax to the cases already reported. I remember very well, as a house officer more than 20 years ago, a patient who had had the left side of the neck explored by one of our senior surgeons. Operation was followed promptly by leakage of milky fluid from the wound. The condition of the patient slowly deteriorated and he died of inanition in a period of approximately four weeks. From that time until World War II, I did not see another case of injury of the thoracic duct. While overseas in 1944, I had occasion to observe a patient who had sustained a perforating wound of the left interscapular region, the site of exit of the missile being in the suprasternal notch. By some miracle, the patient had escaped injury to the trachea and great vessels. Except for the fact that he was intensely dyspneic and cyanotic, he had no complaints. X-ray examination revealed a dense shadow in the left chest; and, at his bedside there was a test-tube filled with fluid which was assumed to be pus. The patient, strangely enough, had no fever. Accordingly, it seemed obvious that he was not suffering from empyema. Furthermore, as the fluid was carefully observed, its chylous nature was obvoius.

Because of the severe dyspnea and cyanosis, the left chest was aspirated and approximately 4,000 c.c. of chylous fluid removed. This was followed by prompt disappearance of dyspnea and cyanosis. I did not know whether anyone had ever administered chyle intravenously before; and, remembering the patient of 20 years ago who had died of inanition, felt that we should attempt to give this patient his own chyle by vein. With great trepidation, we started the slow, intravenous administration of chyle which had been removed from the patient's chest. Much to our astonishment and delight no untoward reaction was observed; and, at the end of a few hours, we had gradually opened the clamp more widely until the chyle was flowing into the vein at a rapid rate. Aspiration of the chest was performed daily and, at the end of approximately ten days the lung was completely re-expanded and the patient well. A few months later we had a case that was practically identical in all details.

I assume that in both cases, the injury must have been very close to the point of junction of the thoracic duct with the left subclavian vein, because it was inconceivable that a missile entering the body close to the scapula, and making exit in the suprasternal notch could have injured the thoracic duct at any other point. Fortunately, conservative treatment, consisting of aspiration of the chest and the adminisration of chyle intravenously, resulted in the recovary of both patients.

DR. MEADE, JR. (closing).—I should like to add one case report from Dr. Robinson, who is associated with Dr. Jones; I had hoped he would be here.

The question of the etiology of chyluria and of chylous ascites, in many cases cannot be explained on the basis of anything I know of at the present time. The use of the lipophylic dyes, I think, is a valuable procedure and I think I shall use them the next chance I have, which may not be for many, many years.

THE SURGICAL TREATMENT OF ROUND TUBERCULOUS PULMONARY LESIONS (TUBERCULOMAS)

COLONEL HUGH W. MAHON (BY INVITATION), AND COLONEL JAMES H. FORSEE
MEDICAL CORPS, DENVER, COLO.

THE TERM TUBERCULOMA

TUBERCULOMA,[9-11] round pulmonary focus,[3] solitary focus of tuberculosis,[12] calcified pulmonary abscess,[8a] Assman focus,[1] Simon focus,[13] and the Ghon nodule[6] are similar in that they all represent the focalization of a tuberculous pneumonia by fibrous encapsulation, appearing as a rounded subpleural pseudotumor located in some portion of the lung. The Assman focus is infraclavicular, the Simon focus is apical, and the Ghon nodule is located usually in the midlung field. The term "cold abscess" is frequently applied to similar nodules in solid organs and tissues; it corresponds to the "unripe" phase of pulmonary tuberculomas.

There is some objection to the use of the term tuberculoma. Dorland[4] defined it as a "neoplasm caused by the bacillus of tuberculosis." But this is too simple and half wrong; it is not a neoplasm, although it is frequently diagnosed as such in the x-ray interpretation of rounded parenchymal densities in the lungs (Holmes and Robbins[10]).

These tuberculous nodules are the result of a chronic inflammatory process of granulomatous type, which follows a characteristic pattern, associated with, but not the exclusive property of, an infection caused by the *Mycobacterium tuberculosis*, for example, infection with *Coccidioides immitis* can produce a nodule identical with those due to tuberculous infection. Webster's dictionary[14] defined tuberculoma as a "localized growth of tissue caused by the bacillus of tuberculosis; a tuberculous nodule." But this would include microscopic submiliary tubercles as well as the largest of the tuberculous nodules, which in this series was 6.0 by 4.5 cm. Obviously a nodule to be considered a tuberculoma must be of a size sufficient to be recognized in roentgenograms, so should be at least 0.3 cm. in diameter to attract attention to it. In this series of 48 tuberculomas the size varied from 1.0 cm. to 6.0 by 4.5 cm.; the average size was 2.1 cm.

Recently reports of mediastinal tuberculomas have appeared in the literature. Blades and Dugan[2] and Grace[7] reported such cases; Blades's case was apparently a hyperplastic reactive tuberculous lymphadenitis and Grace's case a fibrocaseous lymphadenitis. It is not usual to consider an enlarged tuberculous node or a mass formed by conjoined tuberculous nodes as a tuberculoma; otherwise tuberculomas of the neck, axilla, etc., would be a common diagnosis. Apparently the term tuberculoma as applied to the mediastinal nodules implies

From the Laboratory and Surgical Services, Fitzsimons General Hospital, United States Army.

Read at the Twenty-ninth Annual Meeting of The American Association for Thoracic Surgery, New Orleans, La., March 29, 31, 1949.

that some type of tumor was diagnosed preoperatively, and after the pathologist had established the correct diagnosis of tuberculous lymphadenitis, the surgeon and the radiologist acknowledge their mistake by calling it a tuberculoma.

Tuberculomas have been reported in every organ of the body except those which have natural tissue immunity to invasion by tubercle bacilli, for example, the pancreas.

There is an implication in the term "pulmonary tuberculoma" that it is a solitary lesion. The chest roentgenograms give such an impression, but after the lobe, segment, or wedge containing the tuberculoma is removed and examined grossly, smaller similar fibrocaseous nodules will be found in 60 per cent of the specimens as satellites close to or at some distance from the main nodule (Figs. 1 and 7). So "tuberculoma" is a type of fibrocaseonodose tuberculosis in which one nodule is outstanding, attracting the attention of the roentgenologist by its size, its sharp outlines, and the lack of surrounding parenchymal infiltration. It may be found in any portion of either lung; its location in the 48 cases in this series was as follows: right lung 29, with 13 in the upper lobe, 3 in the middle lobe, and 13 in the lower lobe; left lung 19, 13 in the upper lobe, 5 in the lower, and 1 interlobar.

The Ghon nodule, which is the encapsulated primary focus, is rarely a surgical problem. But the increasing occurrence of primary infection in adults, plus the tendency in this age group to delayed retrogression and calcification of the nodule, will bring the primary round lesion to the attention of the radiologist and the chest surgeon.

DEVELOPMENT OF PULMONARY TUBERCULOMAS

It is generally accepted that the pulmonary tuberculoma, excluding the Ghon nodule, is a reinfection lesion acquired by the aerogenous route. It is the structure of the lung with its air spaces and its pleural covering that sets off the tuberculoma of the lung as different in its initial phases from tuberculoma of other organs. This initial phase, whether a primary infection or a reinfection, is a caseous pneumonia of varying extent with tubercle formation somewhat later. The original pneumonia, if successfully handled by the body, clears up, leaving a few visible scars. But the body may be only partially successful in limiting the process by gradually walling in the area of pneumonia by fibrous encapsulation. When followed in serial roentgenograms this walling-in appears as an irregular shadow which gradually rounds out, becomes denser, more homogeneous, and sharper in definition, with the appearance on roentgenograms of that of a discrete round homogeneous density in otherwise fairly normal parenchyma. This is the tuberculoma stage, representing a truce in the struggle between the body and the tubercle bacillus, with the residual bacilli secure behind their fibrous wall. In streptomycin treated cases, assays of these nodules for the drug were negative. The nodule may remain apparently unchanged for years, lulling the doctor into false ideas of its stability and innocence. But in many of the lesions, considered an immature type, there is microscopic evidence that they are sluggishly active; caseation is continuing on the inner side of the fibrous wall, while on the outer side more fibrous tissue

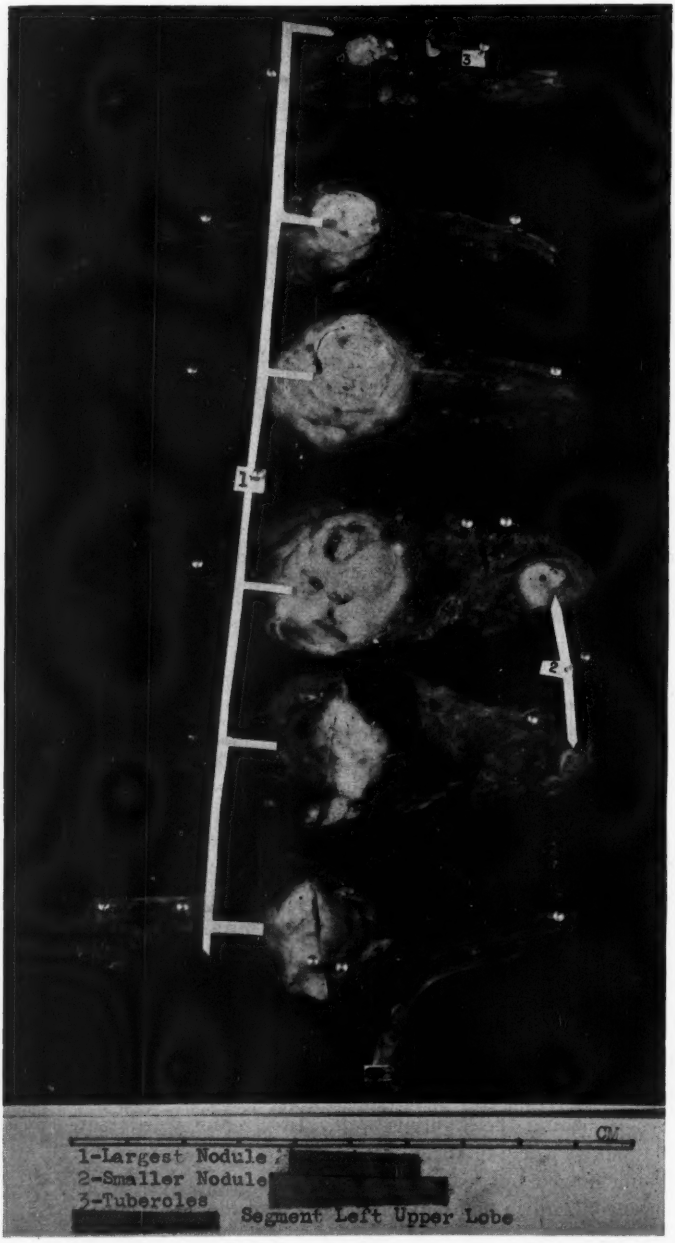


Fig. 1.—Tuberculoma with distant satellite nodules. Material from lesion positive for acid-fast bacilli.

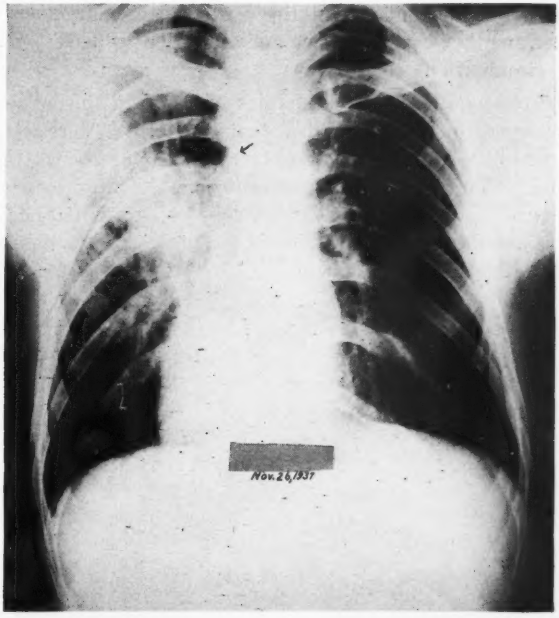


Fig. 2 (Case 1).—Considerable infiltration, left upper lobe. Sputum positive. (See Fig. 4.)

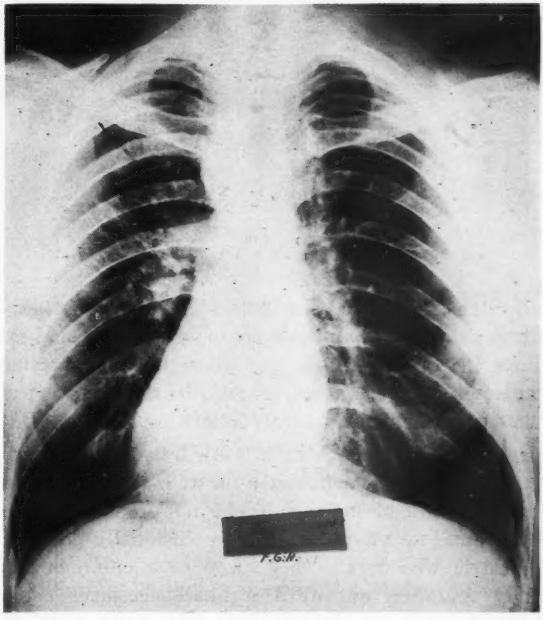


Fig. 3 (Case 1).—Residual rounded density from a tuberculous caseous bronchopneumonia. Lobectomy performed. Caseous tissue of nodule positive for acid-fast bacilli. (See Fig. 2.)

is being added, but the balance in the centrifugal enlargement is so evenly maintained that neither change in size nor alteration in density may be detectable by x-ray examination.

Of the 48 cases of tuberculous nodules reported in this paper, 60 per cent were well-developed round lesions when first observed. There were no available roentgenograms or too infrequent roentgenograms to follow the development of these lesions. The remaining 40 per cent were followed by serial roentgenograms for several years. Observation of the x-ray examinations in this latter group, plus the microscopic examination of the nodules after they were removed, showed three methods of development:

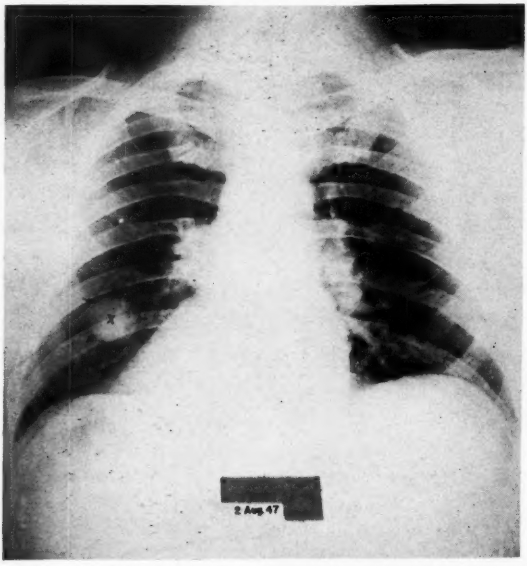


Fig. 4.—Round lesion known to be present and slowly increasing in size for six years. Material from nodule negative for acid-fast bacilli. (See Fig. 5.)

1. Originally there was a rather extensive tuberculous caseous bronchopneumonia with positive sputa and accompanied by the usual symptoms of an active tuberculous infection. Under the usual bed rest regimen, the rather extensive pulmonary infiltration slowly cleared leaving a rounded density much smaller than the original, involved area (Case 1, Figs. 2 and 3).

2. In a clear lung field an indistinct, faint, irregular, hazy spot or a cluster of small (several millimeters) densities appeared. Symptoms were as a rule absent or there was minimal malaise, slight nonproductive cough, occasional 99° F. temperature, and negative sputa, and occasionally positive cultures were obtained from gastric washings. This fuzzy area enlarges and increases in density, gradually rounding out until it finally becomes a sharply circumscribed round shadow. Microscopically the process is a caseous pneumonia but smaller pulmonary units are involved, designated as a lobular or bronchiolar

pneumonia, with each small unit encapsulating and fusing with its neighbor to produce a rounded nodule of approximately the same size as the originally involved focus.

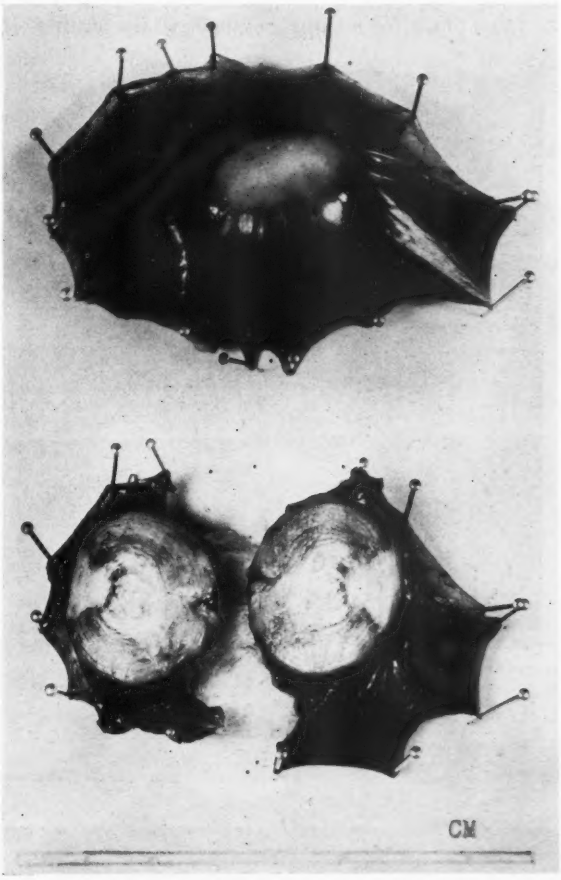


Fig. 5.—"Mature" tuberculoma. Segment of left lower lobe. (See Fig. 4.)

3. It begins as an extensive area of tuberculous bronchopneumonia which proceeds to cavitation. In one-half of such cases it was in the stage of cavitation when first detected by a routine x-ray examination. Occasionally spontaneously, but usually as a result of compression therapy—pneumothorax, pneumoperitoneum, or thoracoplasty—the bronchus which drained the cavity became blocked, and the cavity shrunk, its caseous contents were retained and were concentrated, and gradually the lucency of the cavity lumen was blacked out. The result is a round focus not recognizably different at this stage from the similar rounded foci of 1 and 2, mentioned previously. At the same time the positive sputum was converted to negative.

FATE OF TUBERCULOMA

When the nodule is formed by the encapsulation of broncho or bronchiolar and alveolar caseous pneumonia, the outlines of the consolidated alveoli, filled with ghost epithelioid cells, can be still identified in the microscopic sections. It may persist in this phase for months. Ultimately the outlines of the previous

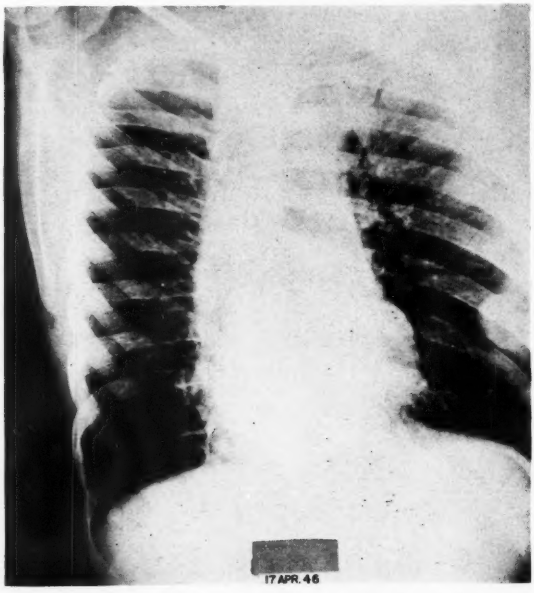


Fig. 6 (Case 2).—Round lesion, right. Asymptomatic. An "unripe" tuberculoma. Material from lesion positive for acid-fast bacilli. (See Fig. 7.)

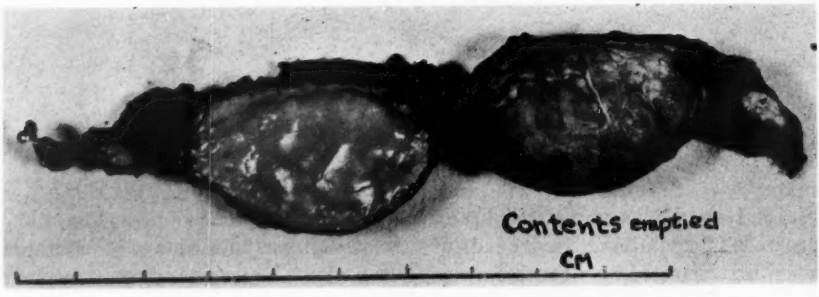


Fig. 7 (Case 2).—"Unripe" tuberculoma. (See Fig. 6.)

alveolar and lobular structure and contained cells disappear and the center of the nodule is uniformly caseous and structureless. The periphery is composed of concentric layers of fibrous tissue with some hyalinization and is infiltrated by plasma cells and lymphocytes. Between the fibrous wall and the caseous

contents there is a narrow zone of epithelioid cells and occasional typical Langhans giant cells, but usually these giant cells appear shrunken and distorted. In places this intermediate epithelioid cell layer is replaced by a narrow zone of granulation tissue. The caseous center tends to inspissate and calcium phosphate is deposited in it. This calcium deposition may be irregularly scattered through the caseous center or be deposited in concentric rings (Liesegang's rings). The calcification in our cases was never as general, complete, and dense as in a Ghon nodule; rarely was decalcification required before the sections could be cut. This targetlike, partially calcified nodule is the "ripe" or mature tuberculoma and smears and cultures of these lesions were always negative for tubercule bacilli (Figs. 4 and 5). The ringlike calcifications may be visible in roentgenograms. Haight and Farris's case[9] was of this type, as were Cases 1 and 2 of Graham and Singer.[8] Such calcified fibrotic nodules are mausoleums erected around dead bacilli.

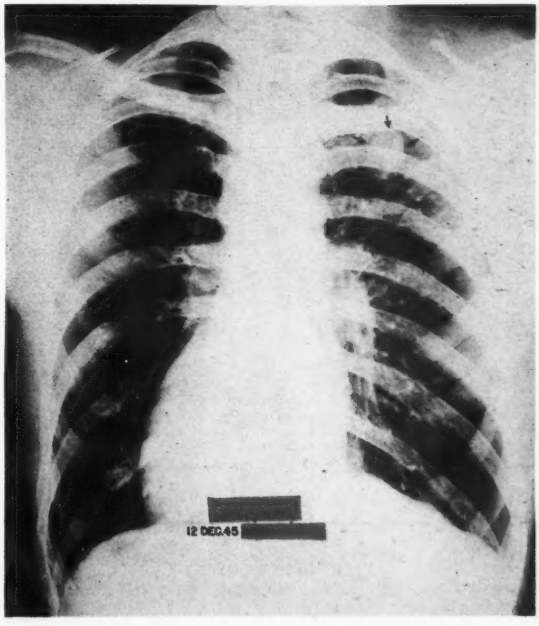


Fig. 8 (Case 3).—Round lesion, right, which cavitated. (See Fig. 9.)

Occasionally the caseous center liquefies uniformly, and the nodule appears as a thin-walled fibrous sac filled with diffluent pale yellow material more like pus than caseous material (Case 2). This type is the most unripe and usually contains innumerable acid-fast bacilli (Figs. 6 and 7). Its removal may be complicated by the spilling of its contents with the possibility of the development of a tuberculous empyema and an infected operative site with pleuro-

cutaneous fistula. In the case of Maurer-Mast and Franklin[11] this occurred. In Case 3 the liquefaction was incomplete; communication with a bronchus was re-established and a thick-walled cavity remained (Figs. 8 and 9).

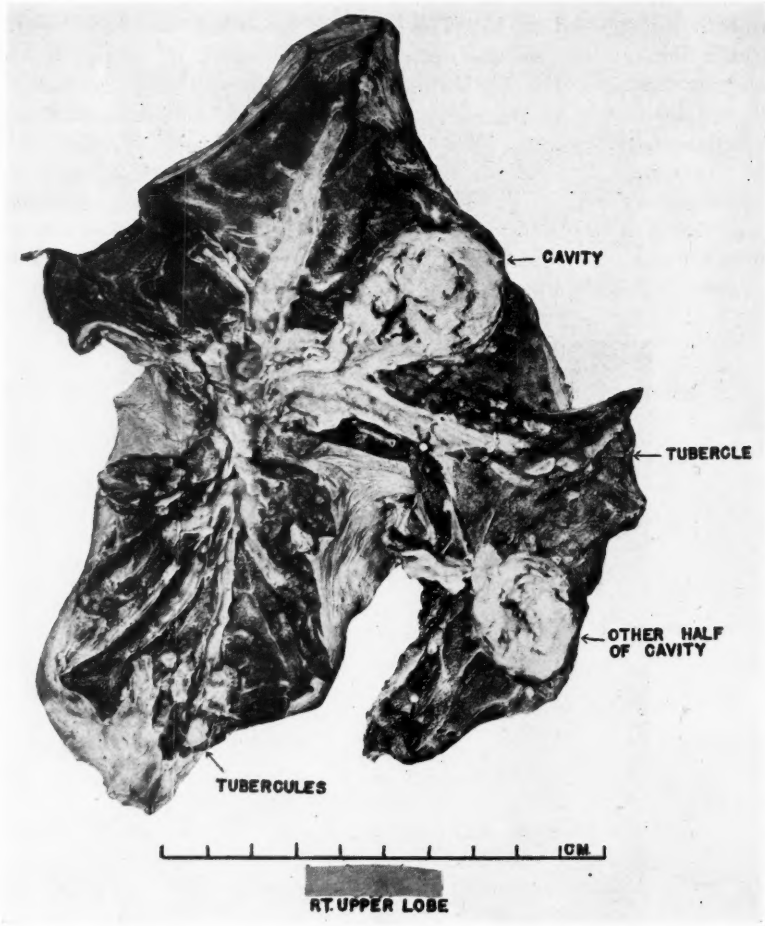


Fig. 9 (Case 3).—Tuberculoma which cavitated and established communication with a bronchus. A tuberculous endobronchial disease is also present. (See Fig. 8.)

Unfortunately the large majority of the solid nodules are slow to calcify and mature; the longest observed in this series was eight years when it began to soften and the sputa became positive. They often show small areas of softening and liquefaction, evidenced in the roentgenograms by small eccentric lucencies which may shift within the nodule when followed by serial roentgenograms. It is rather characteristic that these lucencies are located at the junction of the caseous and fibrous zones and often appear in the x-ray shadows as periph-

eral "slits" following the curve of the wall of the nodule (Fig. 10). Smears and cultures of these irregularly softened nodules are usually positive for acid-fast bacilli. There are always small patent bronchi or bronchioles in close proximity to the wall of the tuberculoma. Often portions of the wall are quite thin. With liquefaction close to a thin wall, communication can be and is establised with the bronchi, with resulting escape of bacilli containing material and reactivation of the tuberculous process.

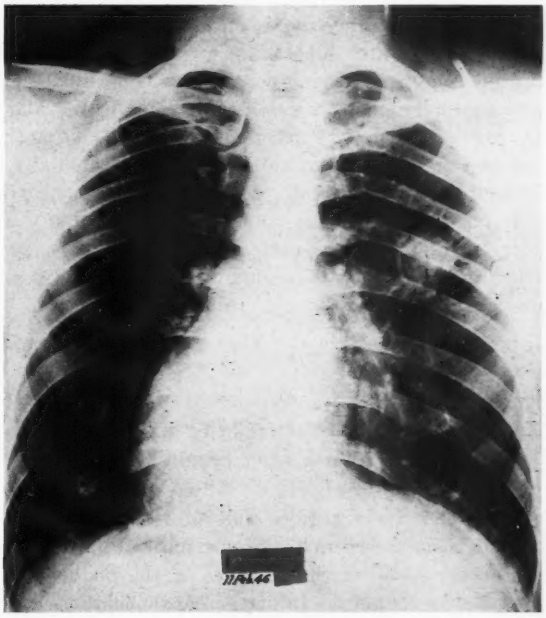


Fig. 10.—Rather rapid enlargement of round lesion, right. Note slitlike space at periphery. Material from center of excised lesion positive on culture for acid-fast bacilli. A "ripened" tuberculoma which has begun to soften and cavitate.

In an occasional slide, submiliary tubercles have been observed in the walls of blood vessels close to the nodule. This infers the possibility of hematogenous spread although no such case occurred in our series.

Tuberculomas originating from encapsulated caseous pneumonia are always close to the pleura in the periphery of the lung. Those that bulge slightly beneath the pleura usually have a white to yellow hyalinized plaque marking the fusion of the wall of the nodule with the overlying reactively thickened pleura. Those that do not quite meet the pleura usually have a dimpled pucker over them with a small white fibrous pleural thickening at the bottom of the dimple. The hyaline plaque often extends as a "V" into the nodule and may be so dense that the nodule is grossly diagnosed as a chondroma (Figs. 4 and 5).

Normal lung tissue surrounds the wall of the nodule. Usually interlobular trabeculae radiating from the wall of the nodule are thickened. Close to the

wall there is a narrow zone of partially atelectatic alveoli, due to compression by the nodule. The lymphocytes and plasma cell reaction usually extend into the slightly thickened fibrosed walls of these alveoli. It is common to find submiliary epithelioid giant-cell tubercles in the surrounding parenchyma as evidence of continued activity of the tuberculous process. As mentioned previously, satellite fibrocaseous nodules 0.2 to 0.7 cm. in diameter may lie close to the main nodule. Occasionally the satellites fuse with the main nodule, explaining the enlargement of some nodules.

The description of a tuberculoma is entirely individual; each one differs. The general characteristics are: (1) a fibrous wall hyalinized in varying degrees; (2) a caseous center of varying consistency from diffluent to dry, granular, and chalky; (3) calcium deposition of varying degree and arrangement; (4) anthracotic pigmentation depending on the degree of anthracosis in the rest of the lung and on the area of the parenchyma originally involved; (5) hemosiderin pigment deposition, usually scanty, and associated with the presence of granulation tissue in the lining; (6) cavity formation of varying degrees, usually irregular, slitlike, and eccentric, rarely completely cavitated; (7) a pleural cap of hyalinized fibrous thickening over the bulging dome or a dimpled area over the deeper tuberculoma.

DIAGNOSIS

As aids in the diagnosis there are:

1. A careful history. But in the majority of cases no history of personal or familial tuberculosis was obtainable nor could any history of definite contact be found.

2. Roentgenograms. It is always well to remember that there is more tuberculosis present than the roentgenograms indicate. Posteroanterior roentgenograms of the chest establish the presence of the nodule and of a calcified Ghon nodule or a Ranke complex. In one case, calcifications were demonstrated in the spleen. Stereoscopic roentgenograms will help in localization. Oblique, lateral, and apical films may better visualize the nodule and locate it fairly accurately. Potter-Bucky technique and tomograms help in better delineation of the nodule and its internal structure, and in locating the depth of the lesion from the chest wall.

3. Fluoroscopy. It will show that the nodule does not pulsate and that it moves with the lung.

4. Bronchoscopy. Its value is chiefly negative. As these nodules are usually at the periphery of the lung they are beyond the limited field of the bronchoscope. If the nodule has cavitated and communicates with a bronchus, bronchoscopy may determine which bronchus is draining and by obtaining material for culture may establish a diagnosis of tuberculosis. Preoperatively it is used to determine if endobronchial tuberculosis is present.

5. Bronchography. It is usually used to rule out other conditions, as bronchiectasis and bronchial cysts. It is the most accurate way to localize the bronchopulmonary segment involved.

6. Skin sensitivity tests are usually not particularly helpful. The tuberculin skin test may be positive; in this group 70 per cent were positive, many only with second strength tuberculin (.005). Histoplasmin and coccidioidin tests may be equally positive. The coccidioidin skin test may be positive and the tuberculin negative, yet the lesion proves to be tuberculosis. In other words, skin tests are as often confusing as they are helpful.

7. Needle biopsy. Although employed by others, it is not used at Fitzsimons General Hospital.

8. Physical examination. It is usually negative. No definite findings as a rule are present except in those cases of a residual nodule following extensive active tuberculosis.

9. Sedimentation test. It is usually normal or only slightly elevated.

DIFFERENTIAL DIAGNOSES

The round lesions found in surgical specimens removed, since 1943, at Fitzsimons were: (1) atelectasis of a nipple of lung parenchyma, adherent to the parietal wall, which had been "strangled" by adhesions; (2) bronchial adenoma not visualized by bronchoscopy; (3) echinococcus cyst; (4) peripheral bronchiogenic carcinoma; (5) peripheral fibrosarcoma with no other primary site established; (6) solitary metastasis of a renal adenocarcinoma; (7) a filled bronchiogenic cyst; (8) a venous aneurysm in the middle of a lower lobe; (9) calcified cast in a cystic bronchiectasis; (10) chondrohamartomas (these are also peripheral subpleural round lesions with suggestion of central cavitation at times); (11) nodular lesions of coccidioidomycosis (their differentiation from tuberculoma depends on the recognition of the spherules in the tissue sections or by culture of *Coccidioides immitis* from the caseous contents); (12) encapsulated interlobar tuberculous pleurisy; (13) pyogenic lung abscess. In spite of employing every possible diagnostic procedure to arrive at a correct diagnosis, each of the aforementioned lesions was suspected at some time during the hospitalization of the patient to be a tuberculoma, and only their examination after removal established the correct diagnosis.

REASONS FOR SURGICAL REMOVAL

1. There is no medical treatment that will clear up these nodules. Streptomycin has no effect on the nodule and from assays on five of these encapsulated lesions, it appears that streptomycin does not penetrate their fibrous wall.

2. They are potentially dangerous. They may persist for years apparently unchanged and then cavitate, break their fibrous barrier with a resulting acute tuberculous pneumonic flare-up.

3. The employment of every available diagnostic procedure may still not establish a correct diagnosis. Only by excision of the lesion and its examination by the pathologist will the specific diagnosis be obtained.

4. Parenchymal round lesions, by the law of averages, are mostly tuberculomas, but they can be neoplasms. Seven of the solid round lesions, removed during the same period as the 48 tuberculomas, were tumors; 4 of these were

malignant (1 sarcoma, 2 peripheral bronchiogenic carcinomas, and 1 metastatic round lesion of a primary renal carcinoma). So of 55 round solid lesions from the periphery of the lung, 4 were malignant, or 7 per cent. Effler, Blades, and Marks[5] in their series of 24 round lesions found 15 per cent malignant and approximately 30 per cent tuberculomas but their series included bronchiogenic cysts and round lesion located in the paravertebral gutter.

5. The cure of the visible disease is possible as it is confined to an area readily accessible to surgery. Its removal can be accomplished by surgical means which will not cripple the patient and can restore his peace of mind and usefulness.

6. The operative risk is low; it is no greater than that of appendectomy. In this series there were no operative deaths. The patients are usually excellent operative risks.

SURGICAL MANAGEMENT

The management of these cases depends on an appreciation of the underlying pathology.

Fortunately these lesions are peripheral, subpleural, with few or no adhesions to the parietal pleura. Palpation of the lung usually can detect the extent of the main nodule and the presence of satellite or additional nodules. Surgical judgment must decide the amount of tissue to be removed. A wedge excision is sufficient for the mature fibrocalcific tuberculoma. A segmental or total lobectomy may be necessary where the area involved is too extensive for a wedge resection. Enucleation is to be avoided due to the possible presence of microscopic tubercles in the adjacent parenchyma.

In this series wedge resection was employed in 30 cases, segmental resection in 2, and lobectomy in sixteen. In 1 case the tuberculoma was located along the line of an incomplete minor fissure and the removal of the upper and middle lobes was necessary.

The danger of postoperative tuberculous pleuritis is slight. It did not occur in any of these cases. Likewise postoperative dissemination of the tuberculous process did not occur. After seven and nine months, respectively, 2 cases developed signs and x-ray evidence of a tuberculous process in another lobe; both cases had lobectomies performed.

Appreciating that tuberculoma is a part of a generalized pulmonary disease, delicate surgical decision is necessary to conserve good pulmonary parenchyma and yet adequately remove the diseased tissue.

SUMMARY

A series of 48 cases of tuberculomas is presented, removed preferably by wedge resection, although segmental and total lobectomy was necessary in approximately one-third of the cases. They were removed at Fitzsimons General Hospital between Jan. 1, 1943, and March 1, 1949.

The term tuberculoma is inexact but usage has made it acceptable.

In three-fourths of the cases the lesion was discovered acidentally by routine chest roentgenograms, taken in the course of examinations for annual

physical check-up, for physical clearance previous to separation from or re-enlistment in the armed service, or during screening on admission to hospital for some other condition.

In known cases of tuberculosis their development was followed by repeated x-ray examinations; they are the end result of a tuberculous pneumonia or of the solidification of a tuberculous cavity during compression therapy.

The 48 specimens illustrate the individuality of the process and the various phases of development from immaturity to "ripeness." The slowness to mature and the tendency to cavitate are emphasized.

The marginal slitlike cavitation is offered as a differential point in the x-ray diagnosis of these lesions and occurred in lesions well on their way to maturity.

The ages varied from 19 to 54 years, average age being 32 years. Forty-three men and 5 women composed the group. This preponderance of men reflects the Army source of the patients. As to races, 45 were white, 1 colored, and 1 Japanese. This bears out the lessened ability of the Negro race to focalize pulmonary tuberculosis.

The potential danger due to the presence of viable bacilli in the majority of the tuberculomas is emphasized (Case 3, Figs. 8 and 9).

The comparative safety of the operative removal of these nodules is reflected by the following facts: no operative deaths, no postoperative tuberculous pleurisy, and no immediate postoperative disseminations.

CASE REPORTS

CASE 1.—This 36-year-old medical officer gave a negative familial history for tuberculosis. In 1930, he had pneumonia with no residuals. About Nov. 8, 1937, a dry hacking cough began with malaise and slight fever. The temperature and cough persisted and he lost five pounds. He was admitted to Walter Reed General Hospital, Nov. 18, 1937. Roentgenographic examination revealed extensive infiltration of the left lung from the apex to the level of the third rib with linear nodose appearance and a suggestion of a cavity. Sputa were repeatedly positive for acid-fast bacilli. He was transferred to Fitzsimons General Hospital on Dec. 20, 1937, and a left pneumothorax was induced Dec. 23, 1937. He gained weight, cough cleared, and sputum became negative by July 18, 1938. He was discharged on Nov. 29, 1939. Smears and cultures for tubercle bacilli were negative. He resumed normal activity and check x-ray examinations showed re-expansion of the lung with some fibrosis in the upper left lobe at the site of previous tuberculosis.

He was readmitted March 11, 1945, because sputa had become positive. Sputa and bronchial aspirations were positive between April and August, 1945. He had increased cough and expectoration and there was an infiltrative process in the left upper lobe, and roentgenogram of the chest on April 4, 1945, showed a circumscribed density in the first left anterior interspace (Figs. 2 and 3). This slightly regressed by Aug. 10, 1945. Sedimentation rate was 4/60. On Sept. 6, 1945, a left upper lobe lobectomy was done.

Pathologic Examination.—Specimen was the left upper lobe weighing 135 Gm. Fibrous adhesions were attached about the apex. A firm 1.0 cm. nodule was located in the upper one-half of the posterolateral segment. It had a fibrous wall enclosing grayish yellow caseous material. Smears were positive for acid-fast bacilli. Calcium was present and cholesterin crystals. A bronchiole lay against the fibrous wall. Occasional satellite tubercles were present in adjacent parenchyma. About this nodule in the apical segment, there were scattered fibrosed tubercles and an occasional conglomerate fibrocaseous tubercle.

CASE 2.—This 23-year-old sergeant of the Air Corps stated that there was no familial tuberculous history. He had a chancre in 1943, adequately treated, with serology negative since treatment. He was in excellent health. In April, 1946, a routine chest roentgenogram during examination for separation from the service reported a 3.0 cm. dense, sharply outlined nodule in the right lung. So he was admitted to Station Hospital, Camp Beale, Calif., on April 7, 1946. Lungs were negative on physical examination. Sputa were negative for acid-fast bacilli. He was asymptomatic and afebrile. Diagnoses were pleural tumor, interlobar encapsulated fluid, and focal pneumonitis. Sedimentation rate was 27/60 on April 10, 5/60 on April 29. Transferred to Fitzsimons General Hospital June 14, 1946. Lungs were negative. Bronchoscopy was negative. X-ray examination of the chest revealed a circumscribed rounded density at level of fifth right rib axillary line. Impression was a tuberculoma or primary neoplasm. Laminagram showed it did not involve the ribs. No skin tests were made. Exploratory thoracostomy was performed and the nodule was removed.

Pathologic Report.—Specimen was a 20 Gm. wedge of lung tissue, measuring 5.5 by 4.0 by 2.6 cm. Tags of fibrous adhesions were attached to smooth glistening pleura. A 4.0 by 3.0 by 2.5 cm. fluctuant nodule occupied most of specimen. A fibrous wall, 0.05 to 0.3 cm. thick enclosed soft, semiliquid yellow caseous material; on evacuating this material the lining was trabeculated, grayish. There was a 1.0 by 0.7 by 0.7 cm. outpocket of the main nodule enclosed by a paper-thin fibrous wall. Smears for acid-fast bacilli were negative; culture was positive. Giant cells and epithelioid cells lined the caseous space; in other areas granulation tissue was present. In the outpocket there was a series of caseous foci with giant cells and submiliary tubercles in the fibrous wall, in the pleura, and pleural adhesions.

Diagnosis.—This was a completely softened tuberculoma in which the original caseous pneumonia proceeded to quick softening—an unripe dangerous type especially when enucleation is used, as it was in this case (Figs. 6 and 7).

CASE 3.—This 24-year-old Negro corporal stated that his father and two sisters had died of "lung trouble." He had no serious illnesses and no previous symptoms of chest disease. In October, 1945, a routine chest roentgenogram during examination prior to separation from service reported a rather sharply outlined density in the right upper lobe with central lucency. He was admitted to Wakeman General Hospital Oct. 29, 1945. On questioning he stated he had lost ten pounds in the past year, had night sweats once or twice a month for past three to four years. Gastric washings were positive for acid-fast bacilli. He had occasionally 99° F. afternoon temperature. On bed rest cavity decreased in size and perifocal infiltration cleared. One twenty-four hour sputum was negative for acid-fast bacilli. Sedimentation rate was 40/60. He was transferred to Fitzsimons General Hospital Dec. 29, 1945. He felt well; execpt for scattered râles and diminished breath sounds over right upper lobe, physical examination was negative. Fluoroscopy reported a rounded 3 by 4 cm. tuberculoma-like density in the fourth right interspace posteriorly. Temperature was normal. Sedimentation rate 10/60. X-ray examination on Feb. 5, 1946, reported cavity had enlarged. Bronchoscopy reported slight stenosis and reddening of the opening of the right upper lobe bronchus. Pneumothorax was unsuccessful due to absence of a free pleural space. A review of film in February, 1943, showed infiltration in the right first anterior interspace which had been missed. By March 10, the tiny central lucency in the nodule had enlarged to 2.0 cm. and stabilized at that size. Coccidioidin skin test 1 to 100 was 3 plus, tuberculin P.P.D. .00002 2 plus. Acid-fast bacilli found in one of three twenty-four hour specimens in January and a seventy-two hour sputum on March 13 was positive. Gastric washings were positive by culture in January and March. Sedimentation rate was 10 and 7/60. On May 2, 1946, the right upper lobe was removed.

Pathologic Report.—Specimen was the right upper lobe weighing 152 Gm.; a thin sheet of fibrous adhesions covered its surface with thick fibrous bands attached to a 2.5 by 1.2 cm. area at the upper border of a parenchymal nodule fill in the vertebral border. There was a 2.7 by 2.5 by 2.4 cm. cavity with 0.5 to 0.9 cm. thick walls in the posterolateral segment. The posterolateral bronchus was filled with caseous debris in which acid-fast bacilli were present. Soft caseous material filled the cavity. There were visible tubercles in the lower

branch of the posterolateral bronchus and a group of 0.2 to 0.5 cm. fibrocaseous nodules surrounded the distal end of the anterolateral bronchus. Microscopically there was calcium deposition in the caseous material clinging to the lining which is granulation tissue in some areas, fibroepithelioid tissue in others. There were fresh submiliary tubercles about and in the wall of the communication posterolateral bronchus. Other tubercles, of varying ages, were scattered in the posterolateral segment and the anterior angle.

Impression.—This was a focalized area of caseous pneumonia in the posterolateral segment, which softened, established communication with the posterolateral bronchus, and ended as a cavity with tuberculous bronchitis of the draining bronchus and slight bronchiogenic spread to the anterolateral segment of the right upper lobe (Figs. 8 and 9).

REFERENCES

1. Assman, H.: Ueber eine typische Form ilolierte tuberkuloser Lungen herde im Klinischen Beginn der Entwcklung, Beitr. z. Klin. d. Tuberk. **60:** 527, 1925.
   Idem: Ueber die infraklavikulären infiltrationen im Beginn der Lungen tuberkulose von jugendlicher Erwachsener, Klinwchonschr. **6:** 2128, 1927.
2. Blades, B., and Dugan, D. S.: Tuberculoma of the Posterior Mediastinum, Am. Rev. Tuberc. **50:** 41, 1944.
3. Bobrowtz, I. D.: Round Pulmonary Focus, Am. Rev. Tuberc. **47:** 472, 1943.
4. Dorland, W. A. N.: American Illustrated Medical Dictionary, ed. 21, Philadelphia, 1948, W. B. Saunders Company.
5. Effler, B., Blades, E., and Marks, E.: Problem of Solitary Lung Tumors, Surgery **24:** 916, 1948.
6. Ghon, A.: Primary Lung Focus of Tuberculosis in Children, London, 1916, J. and A. Churchill, Ltd.
7. Grace, A. J.: Tuberculoma of the Mediastinum, J. THORACIC SURG. **12:** 131, 1942.
8. Graham, E. A., and Singer, J. J.: Three Cases of Resection of Calcified Pulmonary Abscess Stimulating Tumors, J. THORACIC SURG. **6:** 173, 1936.
8 a. Case No. 25432, Case Records of the Massachusetts General Hospital: Tuberculoma of lung, New England J. Med. **221:** 665, 1939.
9. Haight, C., and Farris, J. M.: Tuberculoma of the Lung—Case Report, J. THORACIC SURG. **9:** 108, 1939.
10. Holmes, G. W., and Robbins, L. L.: Roentgen Interpretation, ed. 7 Philadelphia, 1947, Lea and Febiger, p. 249.
11. Maurer-Mast, E., and Franklin, R. N.: Tuberculoma of the Lung, Am. Rev. Tuberc. **43:** 301, 1941.
12. Pierson, P. H.: Solitary Foci of Tuberculosis, Development and Progress; Assman Foci Caseous Nodular Tuberculosis and Tuberculomata, Am. Rev. Tuberc. **45:** 75, 1942.
13. Simon, G.: Sekondare Streuherde der Lunge Insbesundere der Fruhen Spitzenherde, Engel-Pirquet Hdbeh. d. Kindertuberk, Leipzig **1:** 470, 1930.
14. Webster's International Dictionary, Springfield, Mass., 1936, G. & C. Merriam Company.

DISCUSSION

DR. ELMER R. MAURER, Cincinnati.—From a total of nine pulmonary tuberculomas operated upon during the past two and one-half years, I have selected two particular case reports which I would like to present briefly because I think they illustrate well some of the hazards inherent in any program of procrastination or watchful waiting in the surgical management of these so-called quiescent tuberculous lesions (slides).

This is a posteroanterior projection roentgenogram of a 34-year-old white woman who was admitted to the hospital with a history of having been observed for several years because of this lesion which is easily apparent in the upper portion of the right lung. Approximately two to three months prior to admission to the hospital she suddenly developed a chronic hacking cough, which was unproductive and irritating in character. Repeated sputum analyses were negative for acid-fast organisms. There are numerous flecks of calcification seen. I would like to point out particularly this small strand which I think has flecks of calcification in it, connecting this mass with the mediastinum. I think this often is of help in making a differential diagnosis between tuberculous lesions and primary tumors. Lobectomy was decided upon and performed.

This is the postoperative picture; the lower lobe has filled the right hemothorax. This shows the tuberculoma which was of fair size and occupied the anterior portion of the upper lobe. Direct smear demonstrated numerous tubercle bacilli and there was a pure culture of the same organisms obtained on further study. Because of the rather sudden onset of the patient's cough—and the fact that at the time of the anatomic dissection this tuberculous mass was found to be contiguous with a major secondary branch lobar bronchus—I think we can conclude that the irritative cough was probably due to the proximity of this mass to a major bronchus and that rupture was imminent.

This 36-year-old white woman was admitted to the hospital following an attack of syncope and suggestive coronary disease at the place of her employment. Electrocardiographic tracings were entirely normal. Routine x-ray examination of the chest showed a conglomerate mass in the upper lobe of the right lung. Sputum analyses were negative for acid-fast organisms and the patient had no antecedent history whatsoever of cough, hemoptysis, or night sweats. I would like to point out the area of calcification easily seen in the lateral projection. The significance of the calcification was not appreciated until the time of operation. We had anticipated doing a right upper lobe lobectomy and, as you can see, right pneumonectomy was the final procedure. At the time of operation there was extensive calcification of the entire membranous portion of the right upper lobe bronchus, so that no point for adequate amputation and closure could be found. A pneumonectomy was decided upon and, after further examination, calcification was seen to extend up even into the trachea. The right main-stem bronchus was finally divided along an S line high on the trachea between two large calcified plaques; also there was encountered a large calcification extending into the pericardium and a portion of this latter structure was removed with the specimen.

I show this slide primarily to point out the very large calcium plaque on the bronchial stump. This next slide was following thoracoplasty and shows the mediastinum back in normal position. The patient made an uneventful recovery, and has returned to work. A pure culture of acid-fast organisms was obtained from the specimen.

I know of no accurate way in which one can determine either by roentgenographic examination or otherwise the bacterial activity of any of these masses, and I know of no way one can predict exactly when symptoms are going to occur for which reasons surgical excision should be advised.

TRANSTHORACIC THYROIDECTOMY

HERBERT D. ADAMS, M.D.
BOSTON, MASS.

INTRATHORACIC goiter may be defined as that type of goiter in which the goitrous mass lies in the mediastinum entirely below the level of the superior thoracic strait. At the Lahey Clinic nearly 28,000 patients with goiter have been operated on and hundreds of these have been classified as being truly intrathoracic by these criteria. Practically all of these goiters, many of tremendous size, have been removed satisfactorily by the cervical route. This has been technically possible chiefly by the maneuver described by Dr. Lahey of the evacuation of the semisolid colloid central portions of these masses, thereby reducing the transverse diameter of the intrathoracic mass sufficiently to permit the delivery, through the neck, of the remaining peripheral and capsular portions of the thyroid gland. This has been technically feasible and satisfactory in by far the majority of these cases.

There have been three cases in the past few years, however, in which the intrathoracic goiter has been removed transthoracically. Two were approacheed transpleurally because of inability to differentiate the roentgenologic findings in these cases from other types of mediastinal tumors because of their extremely low position in the mediastinum.

When the diagnosis of intrathoracic goiter has been considered, either because of the development of pressure symptoms or because a mediastinal mass has been discovered by routine roentgenologic studies, the differential diagnosis from the other common mediastinal tumors is usually difficult. For the purpose of this discussion of the differential diagnosis between intrathoracic goiter and these other common mediastinal tumors, cases have been selected in which the roentgenograms are very similar in appearance. The smaller, low-lying masses, such as in the first case (Fig. 1, *a* and *b*) may have no apparent extension upward or connection with the thyroid in the neck and may have the characteristic appearance of a dermoid cyst, bronchiogenic cyst, or even a thymoma (Figs. 2 and 3, *a* and *b*). The intermediate sized and less opaque masses (Fig. 4) are represented by the second case and have been confused at times with megaesophagus (Fig. 5, *a* and *b*), and it is wise again to stress the importance of routine barium studies of the esophagus in the differential study of mediastinal tumors. In the extremely large masses (Fig. 6) filling the entire superior mediastinum, roentgenologic studies may be identical with those of mediastinal Hodgkin's disease or arterial aneurysms of any of the great vessels originating from the arch of the aorta. The only roentgen finding differentiating intrathoracic goiter from these conditions is that in intrathoracic goiter there is usually more tracheal and bronchial displacement than in the other conditions and on fluoroscopy it can be seen to ascend and descend

Read at the Twenty-ninth Annual Meeting of The American Association for Thoracic Surgery, New Orleans, La., March 29-31, 1949.

From the Department of Surgery, The Lahey Clinic.

on swallowing. Mediastinal Hodgkin's disease (Fig. 7) should always be considered and associated cervical and other nodal involvement should be carefully looked for and a biopsy done if possible. If a biopsy is not feasible and there is still a good possibility that the disease is Hodgkin's, a therapeutic

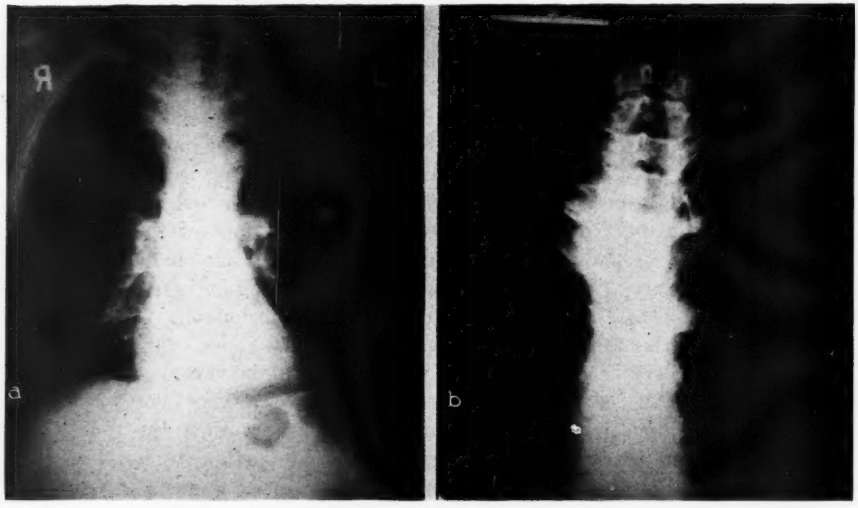


Fig. 1.—Intrathoracic goiter, Case 1. *a*, Low-lying discrete adenomatous goiter in right superior mediastinum. *b*, Bucky film of same, showing slight tracheal deviation to left.

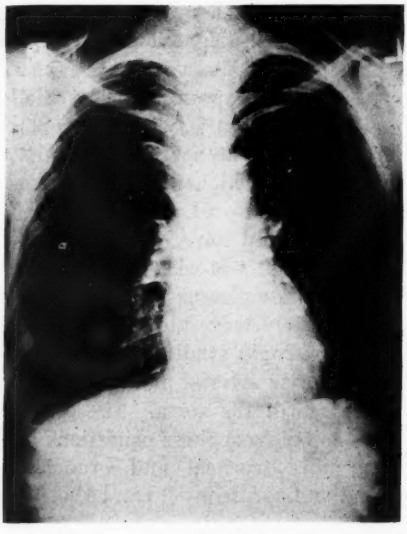


Fig. 2.—Bronchiogenic cyst in right superior mediastinum similar in appearance to goiter shown in Fig. 1.

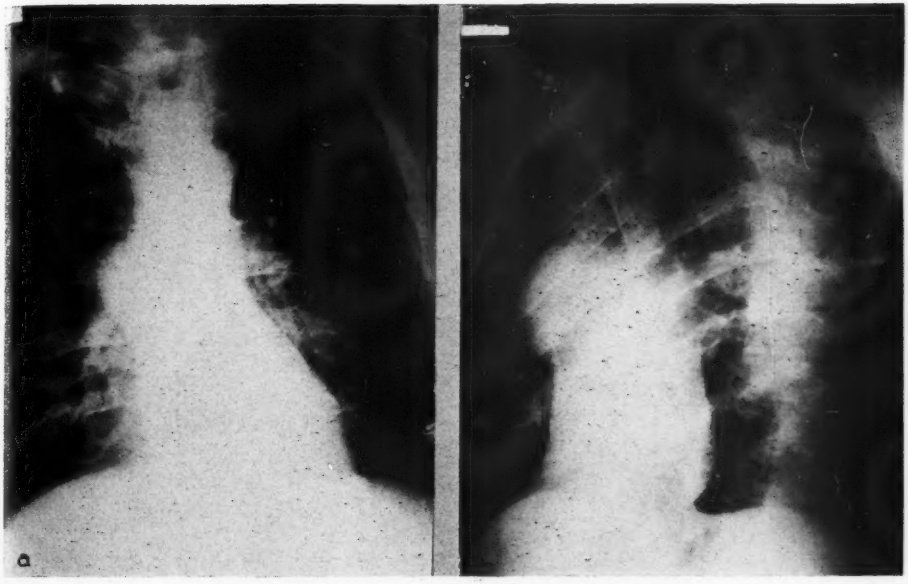


Fig. 3.—Thymoma in right superior mediastinum. *a*, Anteroposterior exposure; *b*, lateral exposure.

Fig. 4.—Intrathoracic goiter, Case 2. Larger goiter mass in right superior mediastinum. Completely intrathoracic, and no displacement of trachea or esophagus.

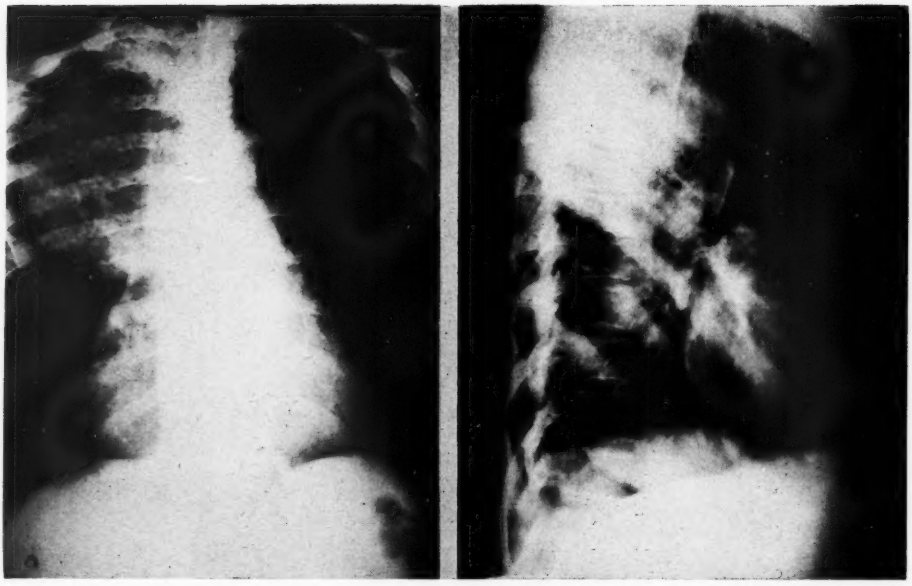


Fig. 5.—Mega-esophagus. Mass in right upper thorax and mediastinum simulating closely that shown in Fig. 4. *a*, Anteroposterior exposure; *b*, lateral exposure.

Fig. 6.

Fig. 7.

Fig. 6.—Large intrathoracic goiter with marked tracheal deviation to the right, removed by the cervical route.

Fig. 7.—Mediastinal Hodgkin's disease.

x-ray treatment may be given, with a rapid regression of the size of the mass being accepted as diagnostic. However, we are in favor of the growing trend toward advising exploration in order to obtain accurate pathologic diagnosis in all of these conditions.

If there are clinical findings such as a bruit over the upper mediastinum, abnormal pulsations in the neck, or altered blood pressure in the upper extremity, or fluoroscopic evidence that this mass could be a vascular lesion (Fig. 8), it is best to carry out angiography to make certain of the diagnosis and determine accurately what vessel is involved. Without this preoperative knowledge and the proper approach, an aneurysm of this type can be easily ruptured during exploration. Such a study would entail retrograde arterial catheterization and an angiogram. Neurofibromas and ganglioneuromas are

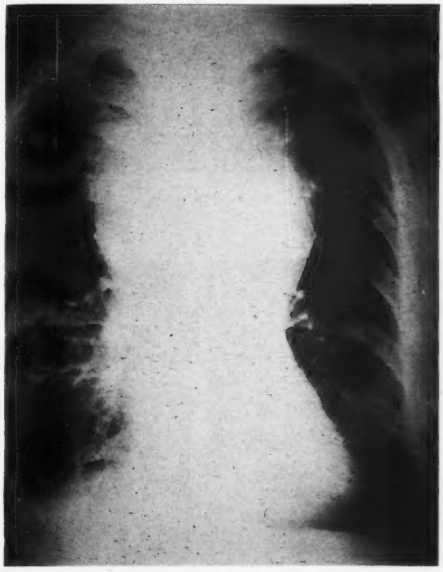


Fig. 8.—Aneurysm of the innominate artery.

common at this level in the mediastinum but lie paravertebrally in the lateral exposure (Fig. 9, *a* and *b*). Teratomas often lie in the same mediastinal plane as goiter, but frequently can be differentiated by demonstrating roentgenologically the presence of bone or teeth in one of the exposures (Fig. 10, *a* and *b*). Having considered all of these possibilities and having done what studies are indicated and possible, however, the differential diagnosis may still be undetermined at the time of exploration.

The larger masses produce lower tracheal and main-stem bronchial compression and the symptoms produced may progress to serious proportions. The third patient was experiencing serious obstructive symptoms and it is well to

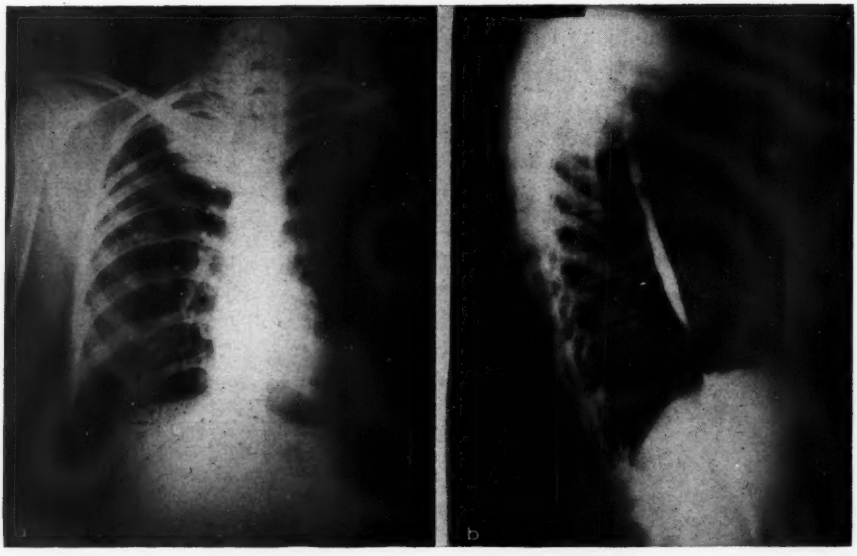


Fig. 9.—Mediastinal neurofibroma. *a*, Anteroposterior exposure; *b*, lateral exposure showing posterior paravertebral position of mass characteristic of this disease.

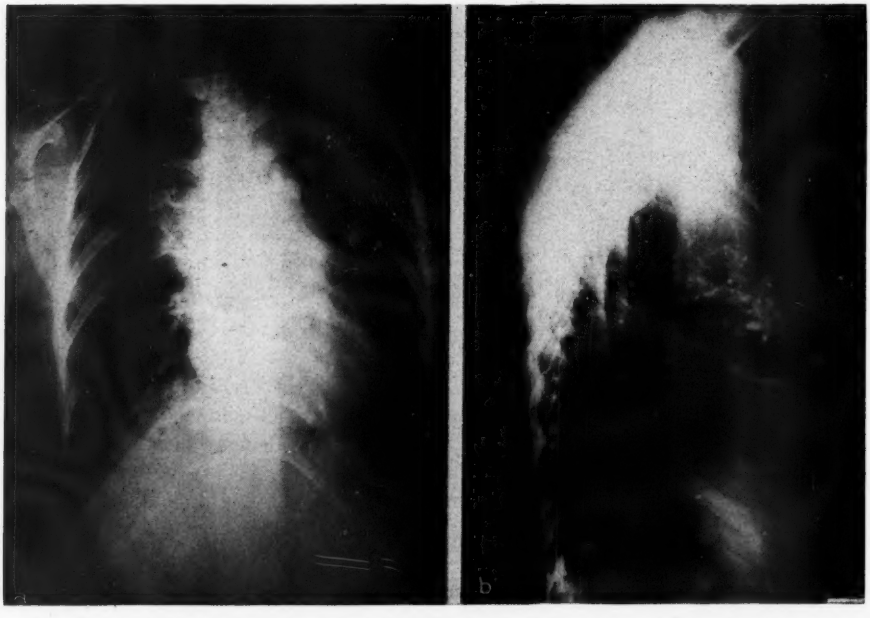


Fig. 10.—Mediastinal teratoma. *a*, Anteroposterior exposure; *b*, lateral exposure showing diagnostic bone and teeth within the mass.

remember that such an obstruction associated with a true, completely intrathoracic goiter cannot be relieved by an emergency tracheotomy since the obstruction is below that point. If the patient is allowed to progress to a critical point of lower tracheal collapse and complete obstruction, it will be too late to do any type of surgery that will be sufficiently rapid to save the patient's life. In these tremendous goiters of this type (Fig. 11, *a* and *b*), the transthoracic resection is a long and hazardous procedure. This is due primarily to their extensive vascularity and their close relationship to the major mediastinal structures. This third patient was operated on by the transpleural approach because of marked obstructive symptoms and because an attempt had previously been made elsewhere to remove the goiter through the neck, with failure, owing to severe hemorrhage encountered and to its tremendous size.

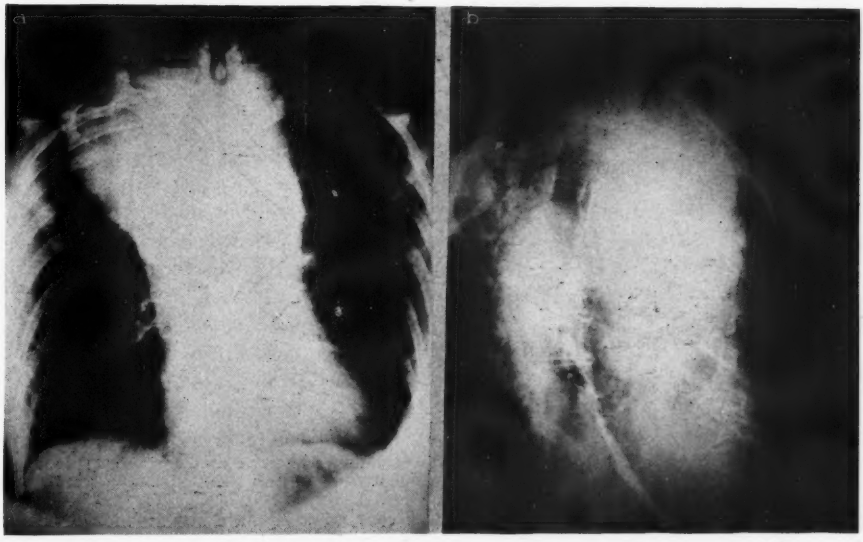


Fig. 11.—Intrathoracic goiter, Case 3. *a*, Tremendous goiter mass filling superior mediastinum and right upper thorax. *b*, Lateral exposure showing the anterior position of the mass.

The anesthetic must be administered by skilled and experienced anesthetists who will be able to cope with almost any type of respiratory obstruction or circulatory collapse throughout this lengthy procedure. Intratracheal anesthesia is used, as in all other types of thoracic surgery.

A posterolateral approach is made, resecting the sixth rib and sectioning the fifth and seventh ribs near their transverse processes, giving a wide exposure of the upper thorax. This transpleural approach is done through the *right thorax* since the greater proportion of the mass extends into this thorax and its mediastinal extension can be dissected under better vision without encountering the aortal arch which would obscure the exposure from the left

side throughout the greater part of the dissection. It is also most probable that it is the aortal arch that limits the extension to the left thorax to some extent. These goiters have extended behind the arch but not often lateral to it. In the huge goiter removed in this manner (Fig. 12), the portion of the mass extending into the upper right thorax was freed subpleurally without much difficulty, with the exception of the management of extensive venous sinuses over the entire surface. The mediastinal portion of the mass was wedged

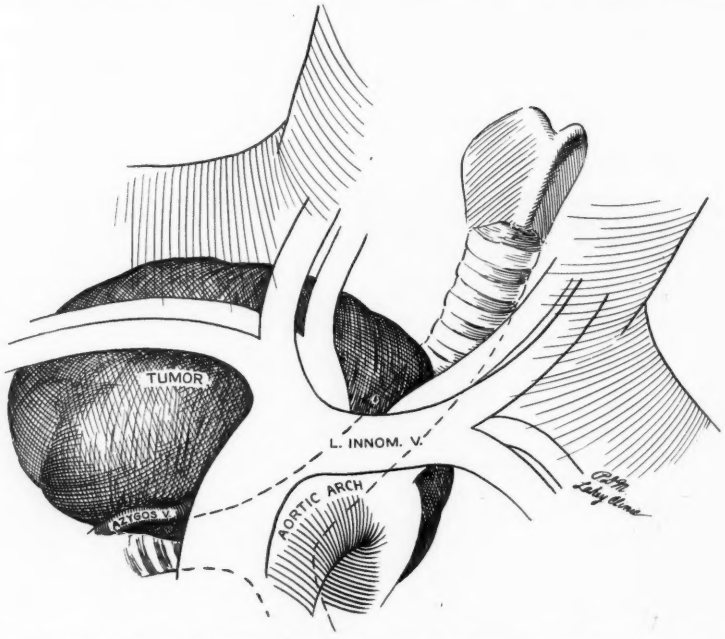


Fig. 12.—Anatomic sketch showing relationship of the intrathoracic goiter (Case 3) to the great vessels and trachea.

firmly in a plane with the lower trachea, carina and main-stem bronchi posteriorly, and the great vessels anteriorly. The right mediastinal exposure showed the mass bulging from behind the superior vena cava and the azygos major vein, compressing these structures anteriorly. The goiter was of such bulk and wedged in so firmly between the planes of the lower trachea and the great vessels that it was impossible to deliver it from the mediastinum safely. In an attempt to apply Dr. Lahey's principle that the center of the mass could be evacuated, thereby reducing the bulk of the mass sufficiently to deal with its capsular remnants more effectively, the mass was broken into with the finger. However, its central portion was of too solid consistency to make this maneuver possible or to reduce the bulk of the mass by evacuating its central portion. In addition to this, marked hemorrhage was encountered within the mass, necessitating packing with Oxycellulose gauze in order to control the bleeding.

It became obvious that some other method of increasing the mediastinal exposure would be necessary if this large mass was to be removed without a fatal hemorrhage. To accomplish this, the azygos major vein was doubly ligated and sectioned, permitting the superior vena cava to be retracted farther anteriorly, and the cleavage plane of the anterior surface of the goiter was then established. There was extensive vascularization at both the superior pole, which is the usual source of the blood supply of intrathoracic goiter, and the inferior pole, with marked venous sinusoidal vascularization of all surfaces. So far as possible the blood supply was controlled under direct vision, but in its more extreme extensions to the left side of the mediastinum and behind the arch of the aorta the cleavage planes had to be followed blindly by blunt dissection with the fingers. Severe venous hemorrhage was encountered and even with the mass finally out of the way, it was impossible to secure this bleeding by clamping, tying, or suturing. It was finally secured with five Oxycellulose packs, measuring 3 by 3 inches. The mediastinal pleura and the thorax were closed, leaving an intercostal catheter for suction drainage of the pleura.

The patient made a good recovery, the lung re-expanded promptly, and there was no late effusion. On the tenth day, however, the patient began to run a septic type of fever, with slight leucocytosis, and by roentgenologic examination the mediastinal shadow remained widened. After some days mediastinal pressure symptoms developed and she was therefore taken to the operating room and a large mediastinal abscess drained through the suprasternal notch. The culture was hemolytic *Staphylococcus aureus*, an infection which was almost certainly superimposed upon a hematoma and the large quantities of foreign material, the Oxycellulose, that was used within this mediastinal space. For these same reasons it is very probable that it would have been good judgment to have drained the mediastinum through the neck at the close of the operation.

CASE REPORTS

CASE 1 (Fig. 1).—The patient was a man, aged 53 years, who had had no symptoms. A mediastinal mass was discovered on routine x-ray chest survey of employees. Physical examination was essentially negative. The roentgen report was of a circumscribed mass to the right of the upper mediastinum and slight deviation of the trachea toward the left. It was elevated on swallowing and did not interfere with the esophagus. There was also enlargement of the left hilar region. The findings were consistent with lymph node enlargement, probably Hodgkin's disease.

At operation, the sixth rib was excised subperiosteally and the fifth and seventh sectioned posteriorly. An adenomatous goiter mass, 7 by 5 by 3.5 cm., lying in the angle between the trachea, superior vena cava, and azygos major vein, was excised. Some large paratracheal lymph nodes were also excised. The pathologic report was multiple colloid adenomatous goiter (70 Gm.) and tuberculous adenitis. The patient made an uneventful recovery.

CASE 2 (Fig. 4).—The patient was a woman, aged 46 years, who had had no symptoms. During a routine check-up examination by the family physician, a roentgenogram of the chest showed a shadow in the right lung field, and further investigation was advised. The

radiologist's report was a lobulated soft tissue mass in the right upper thorax extending out from the mediastinum anteriorly. It did not press on the esophagus or trachea. It could have been an unusual mediastinal thyroid adenoma but was more suggestive of a dermoid.

At operation, a right posterolateral transthoracic approach was made. An adenomatous goiter mass, 9 by 8 by 5 cm., lying above the hilus of the lung, was excised from the mediastinum. The entire blood supply entered at the inferior pole of the mass. The pathologic report was multiple colloid adenomatous goiter; it weighed 190 Gm. The patient made an uneventful recovery.

CASE 3 (Fig. 11).—A woman, aged 53 years, had the chief complaint of rapidly increasing difficulty in swallowing and breathing. Thyroidectomy had been attempted twenty years before entry. Two years previously a substernal goiter was found on roentgen examination. She was told following the previous operation that it was impossible to remove all of the goiter because of severe hemorrhage and the tremendous size of the intrathoracic extension. On physical examination there was moderate stridor and engorgement of the superficial veins of the upper thoracic and cervical region. The radiologist's report was as follows. In the upper mediastinum anteriorly there was a large, sharply circumscribed mass which filled the entire upper third of the right thorax and extended across the midline to the left behind the aortic arch. There was no significant deviation of the esophagus or trachea. This mass showed no pulsation. Impression was a large mass in the anterior mediastinum and right upper thorax with some extension to the left. Lymphoma had to be considered.

The operation and clinical course were as described previously. The pathologic report was multiple colloid adenomatous goiter, measuring 18 by 8.5 by 7 cm. The specimen weighed 700 Gm.

In conclusion, completely intrathoracic goiter is common and even very large masses up to 1,000 Gm., in a large majority of cases, can be removed through the neck by employing Dr. Lahey's maneuver. However, in not all of these cases is it technically possible to use this approach and these will require transthoracic resection. Others that lie particularly low in the mediastinum will also require excision transthoracically because they cannot be distinguished from other types of mediastinal tumors.

The technical problems involved in transthoracic excision of these extremely large completely intrathoracic goiters are chiefly those of obtaining adequate mediastinal exposure and control of the extensive blood supply. Drainage of the mediastinum through the suprasternal notch is advisable.

DISCUSSION

DR. RICHARD H. MEADE, JR., Grand Rapids.—I want to congratulate Dr. Adams for his excellent presentation of this problem, and to emphasize the fact that in certain cases it is impossible to control the blood supply to a substernal goiter through the neck (slides).

This first patient had an ordinary goiter which troubled her a good deal. X-ray examination of the chest showed this extension below. Because she was more concerned with the cervical goiter than the mediastinal one, a combined operation was done with removal of the cervical goiter through the usual incision and the other through splitting of the sternum. It was thought at first that the goiter was continuous, both in the neck and the mediastinum, but we found when we dissected the specimen that they were two separate tumor masses getting their blood supply from two different areas. They were joined by a fibrous membrane. There was no apparent communication between the vessels.

In the next case the problem was very different; here the problem was one of diagnosis. She had a goiter of 34 years' duration, and we knew there was some sternal prolonga-

tion of it, but in addition she had this huge mass here, in the right mediastinum and a small one in the left chest wall. Symptoms were those of mediastinal tumor. The first thing we did was to remove this small, chest wall, tumor mass which proved to be an extrapleural, encapsulated, neurogenic tumor. Several months later the mediastinal tumor was operated on through a posterolateral incision and a huge mediastinal adenomatous goiter was removed. There was no communication between this and the substernal goiter which lay in front of it. You can see from the specimen that it is completely encapsulated above and the substernal goiter came down in front of it.

DR. ARTHUR S. W. TOUROFF, New York.—I would like to point out that since radio isotopes have become available, the diagnosis of intrathoracic goiter can be made in practically 100 per cent of cases. During the past year, our Department of Medical Physics has studied thirty-four anterior and superior mediastinal tumors, of which twenty-one were proved to be thyroid tumors. Twenty of the twenty-one gave positive results on radioactive iodine "tracer studies." The radiologic and clinical diagnoses in these cases included such lesions as aneurysm of the aorta, neurofibroma, dermoid, and esophageal dilatation. There was one case in which an incorrect diagnosis was made. This was a case of very thin-walled colloid cyst in which there was no functional thyroid tissue present. In any mass in which functional thyroid tissue is present all that is necessary to make the diagnosis is to give the patient a dose of radioactive iodine and then pass a Geiger counter over the region of the mass. As soon as one hears the characteristic "clicks," the diagnosis is made.

DR. DERYL HART, Durham, N. C.—I want to report a recent operation, the patient still in the hospital, primarily to urge that if the surgeon is certain that he is dealing with an intrathoracic thyroid which cannot be removed through the neck or if he cannot rule out a thyroid deriving its blood supply from the neck, that the patient be in such a position that the surgeon has ready access to the neck and the chest. It is hard for me to see how the blood supply originating from the thyroid vessels can be controlled through the thoracic approach.

Our patient, aged 79 years, had an intrathoracic tumor, which in seven years had increased only 2 cm. in diameter. On admission she had an intractable cough, complete paralysis of the right vocal cord, almost complete paralysis of the left, and was suffering from severe respiratory embarrassment. It was our impression that the lesion was benign, probably thyroid, possibly a dermoid, but definitely not an aneurysm. Because of the size of the tumor and in the absence of a palpable mass in the neck, it was approached through the right chest, but with the neck exposed. We found it to be thyroid lying posterior to the great vessels. Because of its location and size, I do not see how it could have been removed satisfactorily by splitting the sternum, but it was readily accessible by an anterior right transpleural approach. The tumor in the chest was dissected free and it was determined that there was a pedicle extending into the neck and that all of its blood supply came from the neck.

Through the usual thyroid incision the enormous superior pole vessels were divided and ligated. The thyroid isthmus was split but it was impossible to expose the inferior thyroid vessels or the lateral vein, since the thyroid was anchored to the mass in the mediastinum which prevented delivery or rotation of the thyroid pedicle in the neck. By applying pressure to the mass within the chest and traction on the pedicle in the neck the mass was delivered. This procedure avoided tension on the blood supply. After the mass was delivered, further operative procedure was as for any large thyroid. By this double approach we had the blood supply under control at all times. Her respiratory obstruction was relieved immediately. We have not as yet examined the vocal cords for return of function, but she is making an entirely satisfactory convalescence.

DR. FREDERICK G. KERGIN, Toronto.—There seem to be three groups of patients coming within this general group; one is the patient who has the obvious goiter which is intrathoracic and which it is possible to remove from the neck; but if one fails to do so one may then split the sternum and remove it by combined approach (slide).

This is such a case; due to adherence of the thyroid in the chest and mediastinum, we could not remove it safely, so the sternum was split and it was then removed with ease. The next group are those in which one knows the nature of the tumor, and elects to do a transthoracic approach. Here is a patient who obviously had a goiter lying behind the trachea, a patient of Dr. Robert Janes; in which he elected to do a right transpleural approach and found that the operation was accomplished with ease. Again, there are patients in whom the thyroid presents as an intrathoracic or mediastinal tumor, in which one can suspect its nature but cannot reach it through the neck. In the next case, the tumor lies in front of the heart, with calcification. We diagnosed this as an intrathoracic ectopic goiter, and did a transpleural approach from the right side. The next slide shows a similar case in which the goiter lies in the anterior mediastinum, again with calcificaton, on which we have made this diagnosis but have not yet removed the goiter. I think that with this group there is no chance of reaching it through the neck, and primarily a transthoracic approach must be made.

DR. E. E. AVERY, Chicago.—I had two questions to ask Dr. Adams; the first on how to predetermine the diagnosis of substernal thyroid was answered very nicely by Dr. Touroff. In the future, we shall remember to use radioactive iodine in the differential diagnosis of superior mediastinal masses. The second question deals with the aberrant blood supply to these tumors, and I have two cases from Hines Hospital to illustrate this problem. The first slide reveals a right superior mediastinal mass. The work-up gave no particular indication that this was thyroid tissue. The approach was by the transthoracic route and a large adenomatous thyroid was found which derived its major blood supply from the right subclavian artery.

In the second case, the chest film was similar. The thyroid gland was not enlarged to palpation and the basal metabolism rates were normal. Exploration was done through the transthoracic route, and in this case the frozen section revealed adenocarcinoma of the thyroid. The blood supply to this tumor was derived both from the inferior thyroid artery and a large branch from the right internal mammary.

I want to ask Dr. Adams how often aberrant thyroids were found in the mediastinum in this large series of cases, and what vascular supply has been found to these aberrant thyroids? Perhaps a clue to this answer might be in the morbidity and mortality due to severe hemorrhage following removal of these thyroids through the neck. It seems to me that severe bleeding could be encountered if one of these vessels were torn.

The transthoracic approach is not ideal because the major blood supply is normally derived from the inferior thyroid vessels and the tumor usually extends up into the neck, however, the procedure can be continued through the usual thyroid incision after the transthoracic portion has been completed. Perhaps a more direct attack could be made by the usual thyroid approach and then split the upper portion of the sternum to expose the superior mediastinum.

DR. A. J. GRACE, London, Ont.—There is one point I would like to bring out in presenting one operative case and one post-mortem case in about 3,000 post-mortems at our hospital. The operative case was typical of several that have been presented (slide). The patient was a woman 33 years of age, whose work-up had been done by Dr. F. S. Kennedy—I was called in to operate for an undiagnosed mediastinal tumor. The shadow seen is typical of several that have been shown; after removal it measured about 2 by 2 by 2.5 inches and weighed 50 Gm., and was diagnosed pathologically as a colloid adenoma. There was no connection between it and the tissue above that we could discover. It seemed to be surrounded by areolar tissue, and to lie against the lowest part of the trachea on the right side, immediately against the upper part of the azygos vein.

There was one point in this woman's history; she had had a subtotal thyroidectomy done in a smaller hospital four and one-half years previously. There was no history obtainable; that hospital had burned down when I wrote for records, and the doctor who had performed

the operation was dead. Another doctor in the area wrote to me and said he remembered the case and that he felt she was definitely toxic at the time. One wonders whether there had been any compensatory enlargement of this particular nodule following removal of the goiter in the neck.

The post-mortem case, which Dr. John Fisher of our pathologic department recalled for me, was a woman 66 years of age who had died of cerebral hemorrhage. She had a large distinct mediastinal mass situated low down. She also had a history of having a subtotal thyroidectomy years before for a toxic thyroid, but there was no detailed history with regard to that.

I wonder whether any of the other cases reported—Dr. Adams' cases for instance—have had previous thyroid operations, and what possible significance that might have. It seems strange that both the examples we have encountered have had previous operations performed.

DR. ERNEST JANES, Hamilton, Ont.—This is a report of a patient presented before this Association in 1938. At the age of 28 years, in 1930, she had a thyroidectomy performed because of a toxic adenoma. At that time one adenoma about the size of an orange, retrosternal, was removed through the cervical route. She presented herself again in March, 1938, complaining of dyspnea and tachycardia which had been coming on for about five months. The thyroid was not enlarged. X-ray examination of the chest showed the right side to be opaque, but after removal of 2,000 c.c. of rather blood-stained fluid and replacing it with air, it was possible to demonstrate a large tumor mass in the anterior mediastinum, which was protruding somewhat toward the right. A definite diagnosis was not made but because she appeared slightly toxic she was Lugolized, and in November, 1938, operation was carried out. The approach was made by removing about one inch of the second rib anteriorly, separating the parietal pleura, and then dividing the third and fourth costal cartilages. The ribs were then cracked in the anterior axillary line and a window in the chest thus opened. The parietal pleura was stripped out without tearing it, and an oblong tumor was shelled out from the anterior mediastinum which measured about 6 by 4 inches; a second small one, about 1.5 by .5 inches was removed. No blood supply was encountered, there was very little bleeding, and no blood vessels had to be dealt with (slides).

This slide is shown to demonstrate the size of the tumor, with the smaller tumor lying next to it. The microscopic section shows it to be thyroid tissue.

Whether this is a tumor which migrated from the neck into the chest or whether it should be called aberrant thyroid I do not know. I think the absence of any demonstrable blood supply suggests that it might possibly be an aberrant thyroid.

DR. ADAMS.—I appreciate very much these interesting comments. Briefly, with regard to diagnosis I think Dr. Touroff's suggestion of using radioactivated iodine with a Geiger counter would certainly be a very definite and valuable addition to our diagnostic methods.

With regard to whether these completely intrathoracic goiters are truly aberrant, or whether they have detached themselves from the thyroid in the neck and descended into the mediastinum, I believe it will be difficult to decide definitely as to their origin in any given case. I think, in addition to that, one must be prepared to encounter and to deal with almost any type of vascularity; some of these have had their full supply from the inferior pole, and, as we know, in the majority the major blood supply comes from above. I think it would depend largely on the size and consistency of the intrathoracic extension whether or not you felt you must extend the incision into the thorax. In the medium-sized ones I am sure that splitting the sternum will give very satisfactory exposure. In the extremely large ones I believe the best approach is the right posterolateral transthoracic approach.

One of these three patients had had a previous thyroidectomy; that was the one whose roentgenogram simulated mega-esophagus in appearance, and it was completely unconnected

by any tissue into the neck and the major part of its blood supply entered at the inferior pole, probably representing a true, aberrant intrathoracic goiter.

In regard to bleeding postoperatively, we have had patients with huge intrathoracic goiters removed through the neck who have had postoperative hemorrhages. These necks had to be reopened and the large mediastinal spaces repacked with gauze, some of them several times during the immediate postoperative stage. So if these large intrathoracic goiters are removed through the neck, there is still the problem of vascularity from the inferior pole. One, therefore, has to be prepared to deal with that by some form of packing or pressure during the immediate postoperative stage, as well as to watch those patients with extreme care for the possibility of tracheal compression and obstruction. For these reasons it is probable that more of these large, completely intrathoracic goiters should be removed transthoracically.

MESOTHELIAL MEDIASTINAL CYSTS

Pericardial Celomic Cysts of Lambert

E. C. Drash, M.D., and (by invitation) Harry J. Hyer, M.D.
Charlottesville, Va.

FROM time to time there have appeared in the literature reports of an unusual and interesting tumor. Since it has been designated variously by terms such as pericardial celomic cyst, pleura-diaphragmatic cyst, simple cyst of the mediastinum, springwater cyst, serosal cyst, etc., there is confusion regarding its true nature and origin, although a careful study of reported cases reveals identity in histology, location, and appearance.

During 1946 and 1947, five cases of this type of cyst were successfully operated upon in this hospital. The purpose of this report is to record these cases and to offer suggestions as to (1) pathology, (2) diagnosis, (3) treatment, (4) etiology, and (5) a suitable name for these cysts. Table I lists all cases that can be found in the literature with five new cases.

CASE REPORTS

Case 1.—P. S., a 53-year-old white man, was admitted to the Universtiy of Virginia Hospital July 10, 1946. A routine chest roentgenogram made approximately two years before admission revealed a shadow in the right lower anterior chest. Serial films indicated a slow increase in the size of the lesion, and for this reason, the patient was advised to enter the hospital. The patient had no symptoms referable to the chest.

X-ray examination of the chest showed a well-defined, rounded mass 6 cm. in diameter in close relationship to the right border of the heart, anterior thoracic wall, and right diaphragm. The rest of the chest was clear. Routine physical and laboratory examinations were negative. There was no anemia.

Although it was felt that this was a benign tumor, a bronchoscopy was done to rule out any relationship to the bronchial tree. No abnormalities were noted.

Operation.—A long segment of the right anterior sixth rib was removed and the pleural space entered. A cystic mass was found lying against the right side of the pericardium and the anterior chest wall. It was covered by mediastinal pleura and was easily stripped away from the pericardium. After ligation of several moderate-sized vessels, the cyst was removed intact. The postoperative course was entirely satisfactory and the patient was discharged in good condition eight days after operation.

Pathologic Report.—On gross examination, the cyst measured 6 by 6 by 2 cm., was grayish colored, unilocular, with a smooth wall of soft consistency. It contained clear fluid. Microscopic section revealed the wall to be lined with flat cuboidal epithelium. A few small lymphocytes were seen in the cyst wall.

Case 2.—F. J., a 58-year-old white woman, was admitted to the University of Virginia Hospital on the Medical Service Aug. 15, 1946. She had been in good health until eleven months previously when she suffered a severe attack of pain in the chest. A diagnosis of heart trouble was made by her local physician and she was treated with digitalis. She continued to have pain, dyspnea, and weakness which became progressively worse. The four months preceding admission here were spent in bed. There was no history of cough, expectoration, or hemoptysis.

From the Department of Surgery and Gynecology, University of Virginia.

Read at the Twenty-eighth Annual Meeting of The American Association for Thoracic Surgery, Quebec, Canada, May 31, June 1, 2, 1948.

On physical examination nothing definite was found in the chest. Orthodiagraphic examination revealed a mediastinal tumor on the right side anteriorly. Further x-ray examinations including kymographic studies showed a well-defined rounded mass in the cardiodiaphragmatic angle, projecting outward from the right anterior mediastinum a distance of 8 cm. An electrocardiogram revealed no cardiac abnormality. Routine laboratory studies were negative and there was no anemia.

Operation.—The chest was explored through a right anterolateral approach after resection of the seventh rib. The pleural space was opened and a cystic mass found in the anterior mediastinum adjacent to the pericardium, diaphragm, and anterior chest wall. Adhesions attaching the cyst to the pericardium were broken and the pedicle appeared to lie in fatty tissue between the pericardium and chest wall. After ligation of the pedicle the cyst was removed without difficulty. The postoperative course was satisfactory and the patient was discharged two weeks after operation.

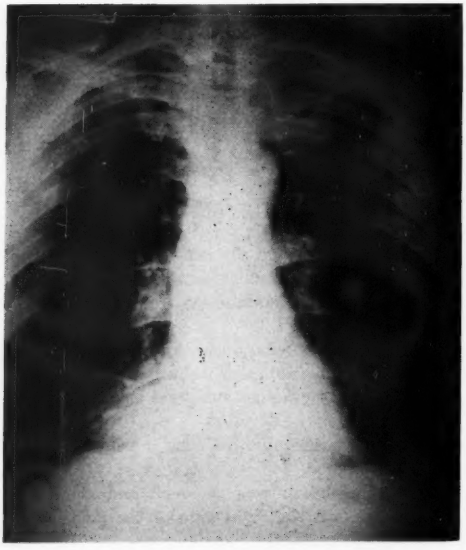


Fig. 1.

Fig. 2.

Fig. 1 (Case 1).—Posteroanterior view showing cyst in right cardiophrenic angle.
Fig. 2 (Case 2).—Posteroanterior view showing cyst in right cardiophrenic angle.

Pathologic Report.—On gross examination, the cyst measured 10 by 8 by 4 cm., was unilocular, with a smooth thin wall of soft consistency. It contained clear serous fluid. Microscopic section revealed a thin fibrous cyst wall lined on the inner surface with flattened mesothelial cells.

CASE 3.—K. Y., a 39-year-old white woman, was admitted to the University of Virginia Hospital on Dec. 9, 1946. About five months before admission she began to have a dry hacking cough which after several weeks became productive of small amounts of yellow mucoid sputum. No hemoptysis, pain, fever, or other symptoms referable to the chest were noted.

On physical examination, nothing definite could be found in the chest. Roentgenologic studies revealed a rounded shadow in the lower portion of the right chest anteriorly which showed no change on serial films. Routine laboratory studies were negative. There was no anemia. An electrocardiogram was reported to be within the limits of normal.

Fig. 3. Fig. 4. Fig. 5.

Fig. 3 (Case 3).—Posteroanterior view showing cyst in right cardiophrenic angle.
Fig. 4 (Case 3).—Lateral view showing cyst in the anterior right cardiophrenic angle.
Fig. 5 (Case 3).—Oblique view showing cyst in the right cardiophrenic angle.

Operation.—The chest was explored through a right anterior approach after resection of the fifth rib. A spherical, thin-walled cyst 4 cm. in diameter was found in the right cardiophrenic angle covered by the anterior mediastinal pleura and attached to the diaphragm. The cyst was easily excised by ligating and dividing the thin attachments and was removed intact. The patient's postoperative course was satisfactory and she was discharged on the thirteenth hospital day.

Pathologic Report.—On gross examination the cyst was thin-walled, globular in shape, 4.5 cm. in diameter, and filled with clear fluid. Microscopic sections showed that the cyst wall consisted of a thin layer of fibrous tissue on the inner surface of which there were a few flattened nuclei suggestive of serosa.

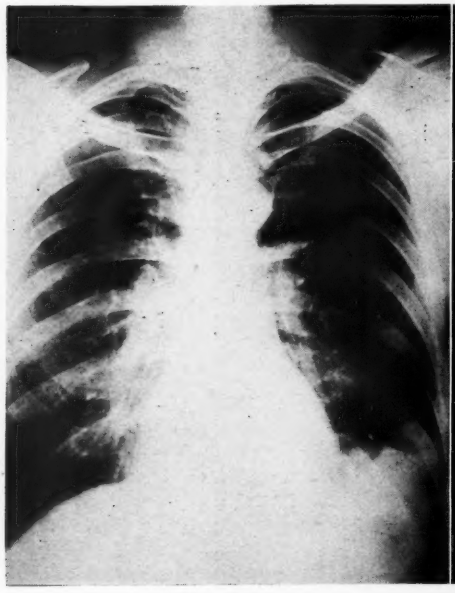


Fig. 6.

Fig. 7.

Fig. 6 (Case 4).—Posteroanterior view showing cyst in the left cardiodiaphragmatic angle.
Fig. 7 (Case 4).—Lateral view showing cyst in the left cardiodiaphragmatic angle.

CASE 4.—V. S., a 37-year-old white man, was admitted to the University of Virginia Hospital on Jan. 20, 1947. He had been quite well until four months previously when he began having indefinite symptoms of fatigue, weakness, and "indigestion" which persisted up until admission to the hospital. He had lost five pounds during this period. There had been no cough, expectoration, dyspnea, hemoptysis, or other symptoms referable to the chest.

Physical examination revealed dullness and decreased breath sounds in the left lower chest anteriorly and posteriorly. Moist râles were heard over both sides of the lower chest posteriorly. No lymph glands were palpable. Roentgenologic studies of the chest showed a large area of increased density in the anterolateral part of the left base. The rest of the lung fields was clear. Comparison with films made in 1932, elsewhere, revealed no change in the lesion. There was no evidence of rib involvement. Barium studies of the esophagus, stomach, and duodenum showed no abnormalities. Four direct sputum examinations and one culture were negative for acid-fast bacilli. Routine laboratory examinations were negative. There was no anemia.

Operation.—On Jan. 25, 1947, under intratracheal anesthesia, a long segment of the left sixth rib was excised and the pleura opened. A large cyst was found at the anterior portion of the left thoracic cage, extending downward and in front of the pericardium. The cyst was subpleural and had bulged the mediastinal pleura laterally. It was excised intact without difficulty after ligating all the vessels approaching the area. The postoperative course was uneventful and the patient was discharged on the eighth postoperative day.

Pathologic Report.—On gross examination, the specimen consisted of a thin-walled, translucent, unilocular cyst measuring 15 by 9 by 7 cm., which contained clear, pale yellow fluid. The lining was smooth and glistening. There were no areas of thickening in the wall. A small amount of lobulated fat was present in the wall. Microscopic examination revealed that the cyst was lined by a single layer of flattened cells resembling mesothelium. The lining was supported by a loose fibrous connective tissue base. No inflammatory reaction was present.

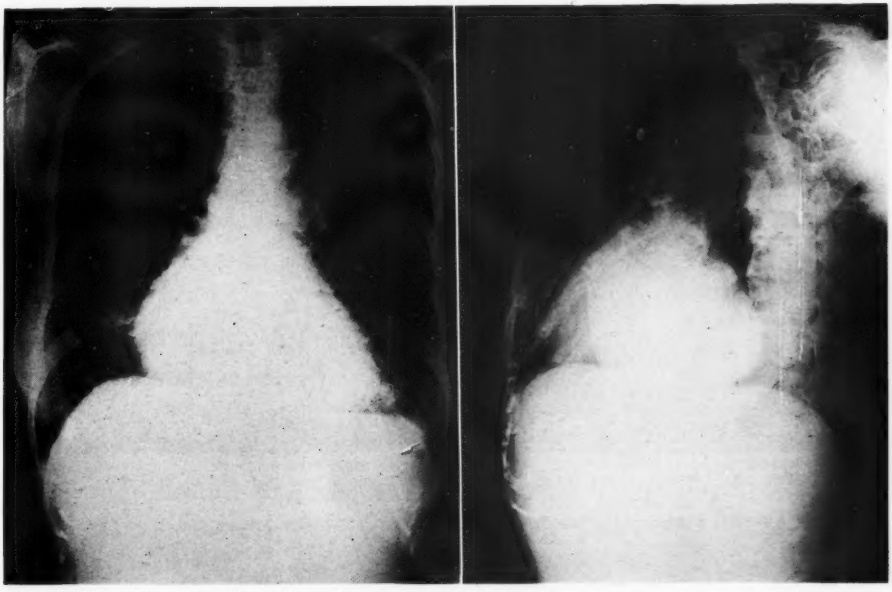


Fig. 8. Fig. 9.

Fig. 8 (Case 5).—Posteroanterior view showing a cyst in the right cardiophrenic angle.
Fig. 9 (Case 5).—Oblique view showing cyst in the right cardiophrenic angle.

CASE 5.—M. A., a 65-year-old white woman, was admitted to the University of Virginia Hospital on June 4, 1947. She had been in excellent health and had had no symptoms except for episodes of "palpitation of the heart," beginning some two years previously. An electrocardiogram at that time in her local hospital was reported to have shown no abnormality. She had not noted any cough, expectoration, dyspnea, pain, wheezing, or hemoptysis. Routine chest films taken six weeks prior to admission revealed a mass in the right chest, and for this reason the patient was referred to this hospital.

Physical examination revealed inconstant moist râles over the right lower chest posteriorly. On roentgenologic examination, a sharply delineated shadow was seen in the right base of the chest. It was of the same density and continuous with the cardiac shadow, projecting 3.5 cm. farther laterally than the usual limit of the right heart border. It was in the anterior portion of the chest and appeared compressed against the anterior chest wall.

Fluoroscopic examination of the chest showed that the mass pulsated synchronously with the heart and could not be separated from it. Routine laboratory studies were negative. There was no anemia.

Fig. 10.—Photograph of large mesothelial-mediastinal cyst removed at operation.

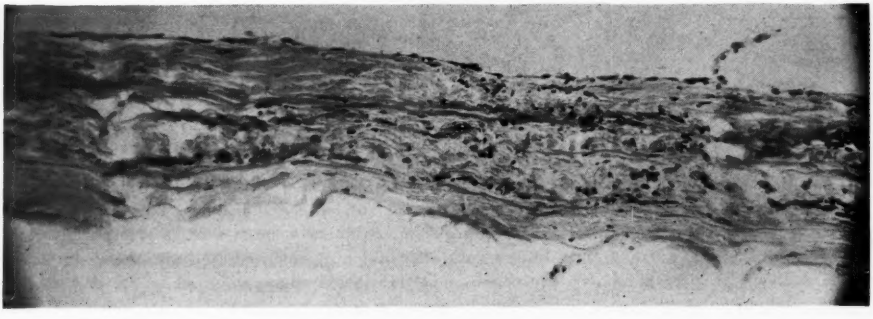


Fig. 11.—Photomicrograph showing section of wall of mesothelial-mediastinal cyst.

Operation.—On June 6, 1947, under intratracheal anesthesia an anterior incision was made over the course of the sixth rib on the right side, the sixth rib and part of the cartilage was resected and the pleural space was opened. There was immediately visible a thin-walled cyst attached to the pericardium and lying in the right anterior mediastinum. The lung was

free and was readily retracted. By dividing the mediastinal pleura over the attachment of the cyst, the latter was easily enucleated without rupture, being peeled off the pericardium for the most part. An additional finding was an anomaly of the right lower lobe which was smaller than normal and was accompanied by very large middle and upper lobes. The anomalous lobe was grossly normal. Convalescence was uneventful and the patient was discharged on the eleventh day postoperatively.

Pathologic Report.—The specimen was a cyst with a transparent wall, measuring 8 by 9 by 4 cm. and containing clear fluid. Microscopic examination revealed a thin, connective tissue wall lined with a single layer of flattened cells similar to those seen lining the pleura. There was also a moderate amount of fat about the wall.

DISCUSSION

Pathology.—Cysts such as those reported in the literature and previously are characteristic in location and appearance. Typically they occur in the cardiophrenic angle adjacent to the pericardium, diaphragm, and anterior chest wall. There is no growth attachment to these surrounding structures, since the cysts are covered by the mediastinal pleura which is bulged laterally by enlargement of the cyst either to the right or left side. They are unilocular, thin-walled, and contain clear fluid. The wall consists microscopically of fibrous tissue lined by endothelial or mesothelial cells which are indistinguishable by ordinary histologic methods.

Diagnosis.—The history is that of any benign tumor arising in the mediastinum. When symptoms are present, they are the common ones of cough, dyspnea, and pain in the chest. They may be attributed to mediastinal compression and vary with the size and location of the lesion and the degree of compression. In only one of the five cases reported were there any chest symptoms; and in this patient, the cough and expectoration were similar to those seen in cases of chronic bronchitis. One other case had severe indigestion. X-ray studies of the gastrointestinal tract revealed no abnormalities and after operation symptoms of indigestion disappeared. This patient had the largest cyst of all, measuring 15 by 9 by 7 cm. and it was located on the left side. Physical findings are inconstant and do not contribute to the diagnosis.

These cysts appear in the roentgenogram of the chest as a smoothly-rounded, usually sharply defined area of uniform density lying against the pericardium, the diaphragm, and anterior chest wall. From a roentgenologic standpoint, these tumors are indistinguishable from many others in the anterior mediastinum. A recent case here, which appeared on x-ray examination to be identical to the five cases reported, was found at operation to be a lipoma.

Differential diagnosis must consider the common lesions encountered in the mediastinum, such as parasitic cysts, teratomas, dermoid cysts, lymphangiomas, lipomas, etc. In most cases a differential diagnosis cannot be made until the chest is explored and the pathologic specimen is examined. Certainly all available means of diagnosis should be employed to rule out, if possible, a malignant tumor. These include, of course, bronchoscopy, bronchography, and sputum studies as indicated.

TABLE I. REPORTED CASES

CASE NO.	AUTHOR	YEAR	AGE (YR.)	SEX	SYMPTOMS AND DURATION	POSITION AND OPERATION	HISTOLOGIC FINDINGS
1	Edwards[7]	1925	30	F	Cough and pain, 7 yr.	Left anterior mediastinum, cardiophrenic angle; cyst removed	Fibrous tissue wall, no endothelial lining seen
2	Dufour and Mourrut[6]	1929	86	M	None recorded	Found at autopsy	Endothelial lining
3	Pickhardt[17]	1931	53	F	Sharp precordial pain, several weeks duration	Left anterior cardiodiaphragmatic angle, cyst removed	Fibrous tissue wall lined by endothelial cells
4	Freedman and Simon[8]	1932	40	M	Abdominal pain, 1½ yr.	Left posterior pericardial angle, found at autopsy	Fibrous tissue wall lined by flat endothelial or mesothelial cells
5	d'Abreu[5]	1933	53	M	Right chest pain, cough, weakness 5 yr.	Right costosternal junction, cyst removed	Fibrous tissue wall with endothelial cell lining
6	Weber[18]	1933	63	M	None recorded	Left extrapleural, found at autopsy	Fibrous tissue wall with endothelial lining
7	d'Abreu	1936	33	M	Right chest pain, dyspnea, 9 mo.	Right costovertebral angle, cyst removed	Fibrous tissue wall lined by flat endothelial cells
8	Case Record[2] Massachusetts General Hospital (No. 23492)	1937	63	M	Stomach trouble 15 yr.	Right anterior mediastinum, cyst removed	Thin wall, no recognizable epithelium
9	Butler by Lambert[15]	1938	54	F	None	Left cardiophrenic angle, cyst removed	Fibrous tissue wall lined with endothelial cells
10 and 11	Berry by Lambert	1940			No symptoms, found on routine x-ray examination	Left cardiophrenic angle, cyst removed	Fibrous tissue wall lined with endothelial cells

12	Case Record[3] Massachusetts General Hospital (No. 26291)	1940		M	Cough, 2 yr.	Left posterior mediastinum, cyst removed	Fibrous tissue wall, no epithelium
13	Greenfield[9]	1941	44	F	Pain in chest	Left anterior mediastinum	Thin wall lined by columnar-cell epithelium
14	Lam[14]	1946	39	F	Angina, dyspnea, and fatigue	Left anterior mediastinum, cyst removed	Fibrous tissue wall, no lining
15	Leahy and Culver[16]	1946	50	F	Hemoptysis, cough, and chest pain	Right anterior mediastinum	Fibrous tissue wall lined by mesothelial cells
16	Curreri and Gale[4]		39	M	Abdominal pain and vomiting, 2 mo.	Left anterior mediastinum, cardiac apex	
17	University of Virginia	1946	53	M	None	Right anterior mediastinum, cardiophrenic angle, cyst removed	Fibrous tissue wall lined with flat cuboidal epithelium
18	University of Virginia	1946	58	F	Weakness, chest pain, 11 mo.	Right anterior mediastinum, cardiophrenic angle, cyst removed	Fibrous tissue wall lined with mesothelial cells
19	University of Virginia	1946	39	F	Cough, 5 mo.	Right anterior mediastinum, cardiophrenic angle, cyst removed	Fibrous tissue wall lined with flattened nuclei
20	University of Virginia	1947	37	M	Fatigue, weakness, "indigestion"	Left anterior mediastinum, cardiophrenic angle, cyst removed	Fibrous tissue wall lined with mesothelium
21	University of Virginia	1947	65	F	"Palpitation"	Right anterior mediastinum, cardiophrenic angle, cyst removed	Fibrous tissue wall lined with flat cells

Treatment.—Because of the many difficulties in preoperative differentiation of intrathoracic masses, exploration should be carried out unless clinical evidence points to a hopelessly inoperable condition. This viewpoint is widely shared by many writers. Harrington,[10] as early as 1929, had removed nine benign tumors and had no deaths or ill effects from the operations. He advocated at that time complete removal of benign tumors in the thorax before they could undergo malignant degeneration or cause death from pressure.

Alexander[1] cautioned against delay in removing intrathoracic tumors and lay particular stress on the circumscribed neoplasm which many physicians assume to be benign and hesitate to remove.

Heuer and Andrus,[11] in a survey of their cases, found that the benign cysts lend themselves to surgical removal and that the size of the tumor is unimportant since very large tumors, though they present mechanical problems, are quite often easily removed with little effect on the patient.

There are three reasons for exploring all intrathoracic masses unless obviously malignant and at an inoperable stage. In the first place, no mass can be confidently considered benign without a biopsy. In the second place, the mechanical effects of a space-consuming lesion on the physiology of respiration and cardiac action must eventually become important and be expressed in symptoms. In the third place, some benign lesions, such as dermoid cysts, may cause complications later by rupture into the bronchus or the pleura. It must be remembered that an accurate pathologic diagnosis cannot be made without exploration. The safety of modern intrathoracic surgery makes this reasoning all the more valid.

Etiology.—At least two theories of pathogenesis have been advanced. Lambert[15] pointed out that during the development of the pericardium there appears early a series of disconnected lacunae in the mesenchyme both lateral and central to the primitive streak. As the embryo develops, these lacunae enlarge, gradually merge, and condense to form the pericardial celom which persists temporarily as an independent cavity. Eventually a connection is formed between it and the pleuroperitoneal celom from which the pleural and peritoneal cavities develop. The ligamentum transversum and ducts of Cuvier close the connection between the pericardial celom and pleuroperitoneal celom, and also divided the pleuroperitoneal celom into pleural cavities above and the peritoneal cavity below. Failure of these normal processes of development have been noted such as the familiar congenital hernia of the diaphragm which results from failure of the ligamentum transversum to divide the pleuroperitoneal celom into pleural and peritoneal cavities. Lambert contended that these reported cysts are probably due to the failure of one of the primitive lacunae to merge with the others and its persistence and development into an independent cavity, forming a cyst. Lambert therefore designated these lesions as "pericardial celomic cysts" and Laipply[13] agreed.

Another explanation of these cysts is suggested by Kindred.[12] He pointed out that the dorsal parts of the pleural cavities are derived from the original dorsal regions of the primitive pericardial cavity. These regions, the pleuro-

peritoneal canals, communicate caudally with the primordium of the peritoneal cavity. Ventrally the borders of the cavities are limited by the primitive septum transversum into which the liver grows and through which the primitive veins enter the sinus venosus of the heart.

Fig. 12.—Section of a 30 mm. human fetus showing beginning fold in the medial wall of the pleural cavity.

As the embryo grows, the lungs begin to form as definite projections from the ventral wall of the primitive pharynx. Coincident with the beginning of the lung buds, the pulmonary ridge, a fold of tissue lying internally to the common cardinal veins at their junctions with the lateral ends of the septum transversum, becomes divided into two folds. The fold growing mesially, ventral to the developing lung, cuts off the pleural cavities from the pericardial cavity by forming the median part of the pleuropericardial membrane. This occurs during the 5 to 10 mm. stage of development. That part of the fold caudal to the lungs grows mesially and closes the communication between the pleural and peritoneal cavities. As a result of these changes, the lungs lie in the primordia of the dorsal parts of the future pleural cavities. These folds, which separate the pericardium from the pleural cavities and the pleural cavities from the peritoneal cavity, are free growing and do not invade semisolid connective tissue to form cystic spaces.

However, beginning at about the 15 mm. stage, the lungs enlarge and with this enlargement the ventral ends of the primitive pleural cavities begin to grow down into the mesenchyme of the lateral body wall between the mesothelium of the pericardial cavity and the ectoderm of the primitive thorax.

Primordia of the ribs and intercostal muscles grow into the mesoderm lateral to the enlarging pleural cavities. Internally, the mesothelium of the pleural cavity comes into close contact with the mesoderm which is external to the mesothelium of the pericardial cavity. Thus, the enlarging ventral parts of the pleural cavities meet opposition as they grow. From such a method of growth, it is conceivable that unequal areas of enlargement may occur and folds may be present in the wall of the advancing pleural cavities. Such folds may be obliterated with later growth, others may enlarge at the same rate as the growing pleural cavity. When the latter occurs, it is possible that such folds may be cut off and form cystic sacs around which connective tissue can be laid down in the same manner of the lamina propria of the pleura. A morphologic condition which lends evidence to this view has been observed in the medial wall of the pleural cavity of a 30 mm. human fetus (Fig. 12). This fold is lined with simple squamous epithelium and is almost cut off from the parent cavity. It forms a narrow fold which cases the surrounding mesenchyme to project into the parent cavity along its ventral lip. If this condition persists, a saclike cyst would develop and could project either into the pleural cavity or the pericardial cavity. Such cysts could occur in any region of the pleura which has been derived from the secondary invasion of the body wall by the pleura. The distribution of the cysts reported have always been found in regions which have passed through morphologic changes during development as described previously.

There seems to be no necessity for assuming that the cysts are derived from persistent infracardiac bursae or their abnormal outgrowths, since cysts derived from such sources would lie in the region of the esophagus, at the central tendon region of the diaphragm. Nor does it have to be inferred that these cysts are remnants of unabsorbed vesicles from which the primitive pericardial cavity is formed. The latter are too delicate and occur too early in development for contribution in the formation of such cysts.

The morphologic evidence available, therefore, suggests that these cysts originate by aberrant growths from the mesothelium of the pleural cavity as it invades the mesenchyme of the body wall. Whether or not hydrostatic pressure contributes to their formation is not known since no measurements have been made of the fluid in the primitive pleural cavities. It has been suggested in the previous discussion that with the separation of the pleural cavities from the pericardial cavity, the pleuropericardial membrane is growing into a free space and is not likely to have its free growing margin modified. However, if the pleuropericardial membrane should grow more rapidly than normal and fold on itself before it fuses with its fellow to form the completed pleuropericardial wall, it is conceivable that a sac could form posterior to the heart in the regions of the great vessels and the bronchi. This region is so compressed during development and the subajacent mesenchyme undergoing so much differentiation into the cartilage of the bronchi and the surrounding musculature, the cysts in this region should be relatively rare. Lambert's theory seems less easy to accept.

Nomenclature.—It is always confusing in the discussion of pathologic lesions when uniform terminology is not employed. In the present instance, this fact is amply demonstrated. In naming a lesion of presumably congenital origin the probable source of the abnormal tissue must be considered. The reason for multiple names for these mediastinal cysts lies in the failure of agreement on pathogenesis. Kindred's explanation of their origin seems a reasonable one. We, therefore, suggest that a name be chosen which recognizes this contribution. The name "mesothelial mediastinal cyst" fulfils this requirement. It is urged that this name be adopted in future reports of this disease.

REFERENCES

1. Alexander, John: J. A. M. A. **119:** 395, 1942.
2. Cabot Case No. 23492: New England J. Med. **217:** 24, 1937.
3. Cabot Case No. 26291: New England J. Med. **223:** 105, 1940.
4. Curreri, A. R., and Gale, J. W.: Ann. Surg. **113:** 1941.
5. D'Abreu, A. L.: Brit. J. Surg. **25:** 317, 1937.
6. Dufour, H., and Mourrut: Bull. et mém. Soc. de med. de hôp. de Paris **53:** 1482, 1929.
7. Edwards, Tudor: Brit. J. Surg. **14:** 607, 1927.
8. Freedman, E., and Simon, M. N.: Am. J. Roentgenol. **35:** 53-56, 1936.
9. Greenfield, I., Steinberg, I., and Touroff, A.: J. THORACIC SURG. **12:** 495, 1943.
10. Harrington, Stuart: Arch. Surg. **19:** 1679, 1929.
11. Heuer, G. J., and Andrus, W. D.: Am. J. Surg. **50:** 146, 1940.
12. Kindred, J. E.: Personal communication.
13. Laipply, T. C.: Arch. Path. **39:** 3, 1945.
14. Lam, Conrad R.: Radiology **48:** 239, 1947.
15. Lambert, Adrian: J. THORACIC SURG. **10:** 1-7, 1940.
16. Leahy, L. J., and Culver, G. J.: J. THORACIC SURG. **16:** 695, 1947.
17. Pickhardt, O. C.: Ann. Surg. **99:** 814-816, 1934.
18. Weber, Parkes: Brit. M. J. **1:** 851, 1934.

DISCUSSION

DR. GEORGE F. SKINNER, Saint John, New Brunswick.—I have been intensely interested in this discussion, because in October, 1936, in the Journal of this Association, we reported a case obviously similar to this one, under the title of "Mediastinal Cystic Lymphangioma." We were not entirely satisfied with this diagnosis in spite of the fact that it was supported by several pathologists including Tumor Registry. At that time we could find no similar case in the American literature although the possibility of such a tumor was mentioned. There were a few reports in the German literature.

A 4-year-old boy was admitted on account of respiratory embarrassment. The entire right side of the chest was filled. After aspirating the pleural fluid, two-thirds of this side was seen to be filled with a multiloculated cystic tumor. On exploration the tumor was found to be composed of numerous cysts ranging in size from 1 mm. to 10 cm. It was easily separated from the upper mediastinum, the vena cava, the pericardium, and from the lateral portion of the diaphragm, but in the angle between the pericardium and the diaphragm very small cysts appeared to infiltrate into the tissues. In spite of being forced to leave small cysts in this angle the boy was well and showed no sign of recurrence when examined ten years after the operation.

DR. CONRAD R. LAM, Detroit.—I should like to present a case which will show the development of such a cyst, in a patient 28 years old at the time of this roentgenogram, who was operated on ten years after these films were made (slides). Three years later, the shadow had increased in size and a diagnosis of congenital heart disease was made. Later, the patient was kept in bed because she was presumed to have a tremendously enlarged heart. The cyst was easily removed through a right sixth interspace incision.

With regard to the suggestion that there be a change in the nomenclature, I call attention to the fact that these cysts are close to if not attached to the pericardium and someone may suggest that they be called "para-pericardial" cysts.

DR. F. A. HUGHES, JR., Memphis, Tenn.—I would like to mention that the thoracic surgery staff at Kennedy General Hospital (Army) removed 14 of these cysts. One was in the left upper mediastinum. Twelve were diagnosed on routine x-ray examination and were asymptomatic. This group formed 20 per cent of the benign mediastinal tumors removed by the Army group. None of the cysts showed a connection with the pericardial space.

DR. GUSTAF E. LINDSKOG, New Haven, Conn.—We have seen two of these anterior cystic lesions in the last year; one multilocular and one unilocular. They show in the wall definite histologic evidence of smooth muscle tissue and a mesothelial type of lining. I do not believe the pericardium contains any smooth muscle; if they were of pericardial derivation, one would not expect that they would show smooth muscle. These were deeply attached in the anterior costophrenic angle, and we suspect their origin from anterior, lymphatic channels.

DR. PLIMPTON GUPTILL, Rochester, N. Y.—I would like to show a couple of slides showing findings very similar to those Dr. Drash showed. These were two men in the middle fifties, asymptomatic (slides).

There is anterior displacement of the esophagus. There is a tumor 8 cm. in diameter with a small projection on the right side.

It has been suggested by Mallory that they may have had an epithelial lining which was destroyed by pressure of the contents. The fluid content in both these cases was clear; chemical analysis was not made.

DR. FRANK B. BERRY, New York.—I have had two of these cases and the structure of both was as shown in the last slides. No smooth muscle was found in either one. Recently at The Veterans Hospital one was removed by Dr. Wylie, and it is the only one I know where a connection with the pericardium was found. It was a typical cyst filled with the same kind of fluid and the opening in the pericardium was pre-existent, because it was seen communicating with the pericardium by a very small stalk with patent lumen.

DR. DRASH.—We suggested that the term pericardial cysts be dropped, because in none of our cases nor in any that we could definitely identify in the literature was there any communication with the pericardium. I am not sure that Dr. Berry's case belongs in this group. His case sounds as if it might have been a diverticulum of the pericardium. In all of the cases that we operated upon the cyst came away quite freely. It had a very limited blood supply and they were all covered by mediastinal pleura and apparently originated in the mediastinum. We felt that the term mediastinal cysts should be used rather than the term pericardial cysts. All of these tumors were against the anterior chest wall, but showed no connection with it.

INTERCOSTAL INCISION IN TRANSPLEURAL OPERATIONS

JOSEPH A. WEINBERG, M.D., AND (BY INVITATION) ALVIN R. KRAUS, M.D.
VAN NUYS, CALIF.

WIDENING of the scope of thoracic surgery has directed attention to the lessening of morbidity as well as mortality. The type of incision for approach to the thoracic cavity, though seldom viewed as a major problem, has an important bearing on the morbidity attending thoracic operations.

In almost all surgical procedures in which the pleural cavity is entered, it is the practice to remove one or more segments of rib or at least to divide one or more ribs posteriorly. This method has been responsible for much of the intercostal neuritis, pneumonitis, and pleural effusion that is so common in any large series of thoracic operations.

In an effort to lessen morbidity, shorten the time of operation, and preserve the normal contour of the thoracic wall, we have used the intercostal incision in a variety of indications for thoracotomy. The results have been impressive. This type of approach has been found to be universally applicable and is now used routinely by us in pneumonectomy, lobectomy, segmental pulmonary resection, drainage of acute empyema and pericardial empyema, decortication of the lung, repair of the diaphragmatic hernia, transthoracic vagotomy, and transdiaphragmatic splenectomy. It has also been used in resection of the proximal two-thirds of the stomach and distal esophagus. Other members of our staff have used this same approach in thoraco-lumbar sympathectomies.

The advantages of the intercostal approach are more than facilitation of opening and closing the thoracic wall. A comparison with cases in which resection or posterior division of a rib was performed reveals a definite difference in morbidity, with a lower incidence of pneumonitis, pleural effusion, and postoperative intercostal neuritis with intercostal incision. A further advantage to the patient is the preservation of the normal contour of the thorax.

Intercostal pain is almost a constant factor with costal resection for exposure of the pleural cavity. This is due to irritation of the intercostal nerve by the sharp edge of the cut rib. Grimson,[1] in a report on 144 thoracotomies in which ribs were resected, stated that all patients had pain in the chest, which was most intense during the second week after operation. This intercostal neuritis is such a common sequel to thoracotomy that some surgeons crush the intercostal nerves above and below the incision[2] or inject them in order to lessen postoperative pain. In Grimson's series, the intercostal nerve inferior to the incision was routinely excised or avulsed and in some patients the intercostal nerve adjacent to the incision was crushed; in others they were injected with alcohol. None of these procedures effected definite relief. In addition to being an objectionable feature per se, the pain also tends to cause splinting of the

From the Department of Surgery, Birmingham Veterans Administration Hospital.

Published with the permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinion expressed or conclusions drawn by the author.

Read (by title) at the Twenty-eighth Annual Meeting of The American Association for Thoracic Surgery, Quebec, Canada, May 31, June 1, 2, 1948.

thorax and limitation of excursion of the thoracic wall, thereby encouraging retention of pulmonary secretions with its resultant atelectasis and pneumonitis. Grimson referred to a form of bronchitis associated with dyspnea produced by accumulation of tenacious mucus in the trachea in fifteen cases of his series. This seemed to be associated with pain and splinting of the thoracic wall and interference with coughing.

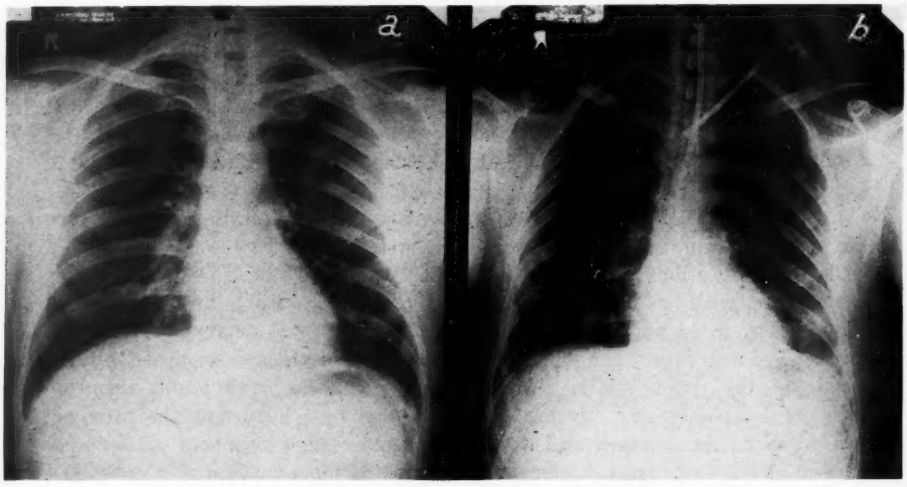


Fig. 1.—*a*, Preoperative chest roentgenogram. *b*, Chest roentgenogram two days postoperative, transthoracic vagotomy, showing slight obscuration of left costophrenic angle.

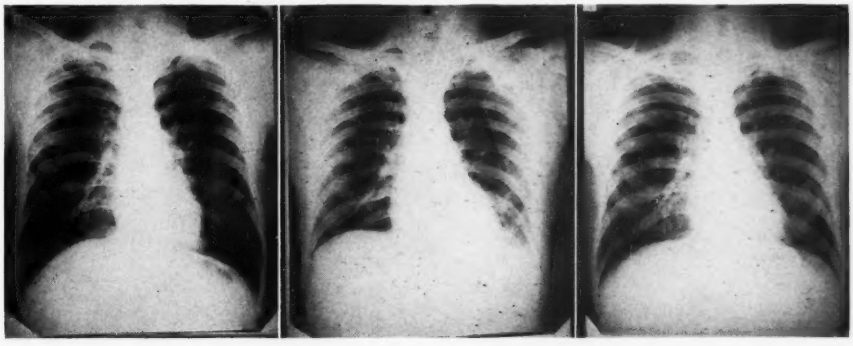
It is possible in most cases of intercostal incision to obtain accurate closure of the pleura, an accomplishment which is practically impossible with rib resection. The practice of approximating the ribs above and below the resected rib by encircling sutures, which is frequently resorted to, is surgically unsound because of the pressure of these sutures on the intercostal nerves and vessels and on the bone itself. There is good reason to believe that inaccurate closure of the pleura is conducive to pleural effusion in the closed thorax. The fluid of trauma and inflammation, which is a necessary consequence of a long thoracic wall incision, is drawn from the thoracic wall into the pleural cavity by the pumplike action of the lungs in respiration, if a pathway for the escape of the fluid exists.[3] With tight closure of the pleura, the escape of the fluid into the free pleural cavity is definitely minimized as shown by follow-up x-ray studies in such procedures as thoracic vagotomy and repair of diaphragmatic hernia (Figs. 1, 2, and 3).

In four patients who had exploratory thoracotomy for nonresectable carcinoma of the lung who have come to autopsy some months later, there was accurate healing with almost imperceptible pleural scar.

The location of the intercostal incision depends upon the operation to be performed. An incision in the fourth or fifth interspace extending from the

midscapular line to the costochondral junction is useful for pneumonectomy, resection of the upper lobe, and pulmonary decortication. If the incision is carried more anteriorly, the internal mammary artery is exposed to avoid accidental injury to it. Apical segmental resection is best performed through the third or fourth interspace.

The seventh or eighth interspace is satisfactory for vagotomy and the eighth is used for such procedures as repair of diaphragmatic hernia and trans-



a. *b.* *c.*

Fig. 2.—*a*, Preoperative chest roentgenogram. *b*, First day postoperative, repair of diaphragmatic hernia, showing obscuration of left costophrenic angle. *c*, One week postoperative, shows complete clearing of the left pleural cavity.

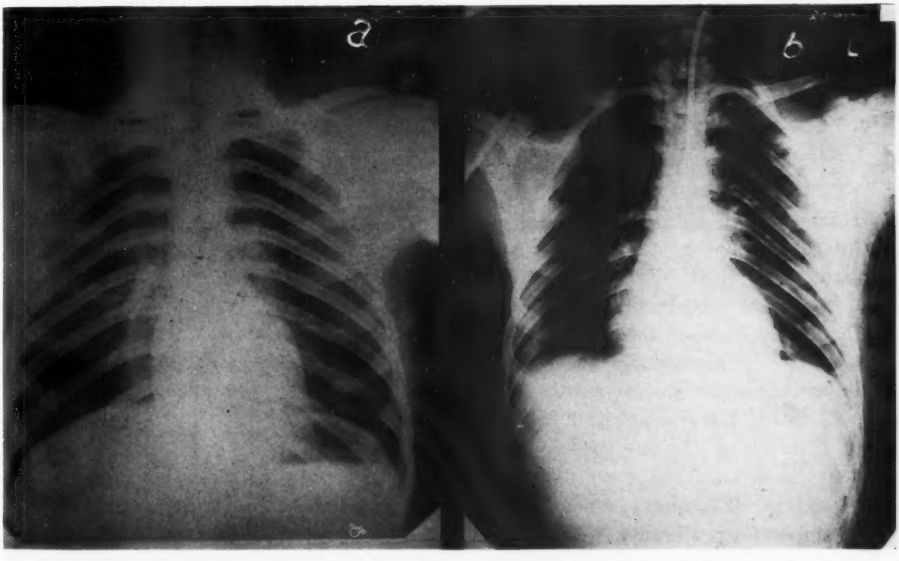


Fig. 3.—*a*, Preoperative chest roentgenogram. *b*, Chest roentgenogram two days postoperative, transthoracic vagotomy. No evidence of pleural effusion.

diaphragmatic operations upon viscera in the left upper quadrant of the abdomen.

In our only case of suppurative pericarditis, in which the pericardial sac was opened into the pleural cavity, the seventh interspace did not give satisfactory exposure because of a relatively high adherent diaphragm, and the seventh rib was therefore divided anteriorly.

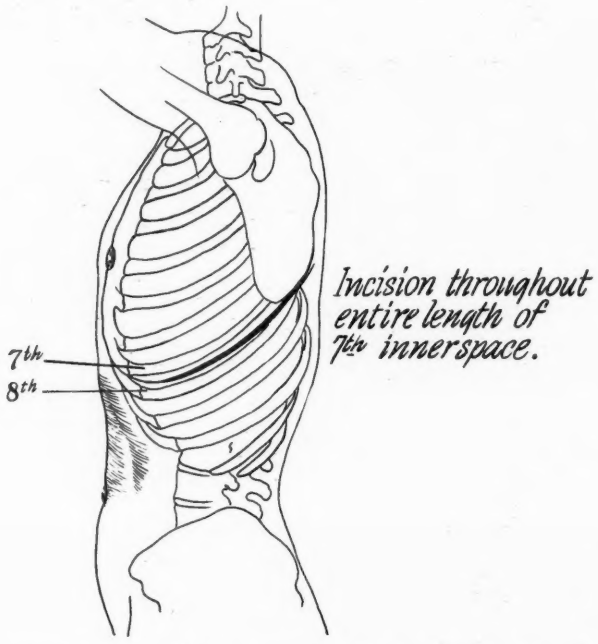


Fig. 4.—Incision is made midway between two ribs in the selected intercostal space.

The seventh interspace is generally the most satisfactory for long incisions. Difficulties with blood vessels are more likely to occur in the region of the interdigitations of the serratus anterior and external oblique muscles in the eighth and ninth interspaces. However, this should in no way deter one from using either the eighth or ninth interspace when indicated. The lower part of the thorax between the seventh and ninth ribs is relatively free of thick muscle tissue except posteriorly, where transection of a relatively small portion of the latissimus dorsi muscle suffices for adequate exposure. The thinner muscles, such as the serratus anterior and the external oblique, are split in the direction of their fibers. As one goes cephalad and posteriorly, more extracostal muscle tissue is encountered, and this together with the scapula increases the amount of dissection. Therefore, when the approach is elective, the seventh or eighth interspace is preferable.

There will be occasions in which one fails to select the proper interspace for the most advantageous exposure, as occurred in three of our early cases. In

such instances exposure is improved by dividing the rib above or below the incision through its costal cartilage. Anterior division is preferable to the posterior because of less irritation to the intercostal nerve. One centimeter of cartilage is resected to lessen the discomfort occasioned by friction of the divided segments.

Fig. 5.—Thorax opened with incision in intercostal space for decortication of lung. Distance between blades of rib spreader (Finochietto) measures 15 cm.

TECHNIQUE OF OPERATION

The patient is placed in a lateral or semisupine position and an incision from 10 to 14 cm. in length is made through the skin in the selected intercostal space. The overlying extracostal muscles are divided with scalpel or by blunt dissection in the direction of their fibers. The intercostal muscles and parietal pleura are divided with a single incision exactly midway between and parallel to the ribs above and below, thereby avoiding the intercostal vessels and nerve (Fig. 4). A heavy nonyielding rib spreader (we have found the Finochietto instrument to be ideal) is then inserted between the ribs over gauze pads which serve to protect the intercostal structures from excessive pressure of the spreader. The rib spreader is placed away from the anterior aspect of the incision in order to lessen the tendency of the costal cartilage to become dislocated from the sternum. While this has caused no difficulty

on the few occasions that it has occurred, it is possible that the anterior edge of the dislocated rib might injure the internal mammary artery. The ribs are then spread slowly, to allow for accomodation of the thoracic cage. An incision from the costochondral junction to the midscapular line will permit an exposure of at least 15 cm. between the ribs (Fig. 5).

After the operation within the thorax is completed the rib spreader is removed and interrupted No. 40 cotton sutures are placed through the pleura and intercostal muscles approximately 7 to 8 mm. apart (Fig. 6). The ribs are brought together by means of a rib approximator and the previously placed sutures are tied. If closed suction is to be maintained after operation, catheters are placed through separate stab wounds. If no postoperative suction is contemplated, a No. 24 urethral catheter is left in the interspace at one end of the wound and the lung is inflated to expel air from the pleural cavity. The catheter is withdrawn just before the last suture through the intercostal muscle and pleura is tied. The extracostal muscles and skin are then closed in layers.

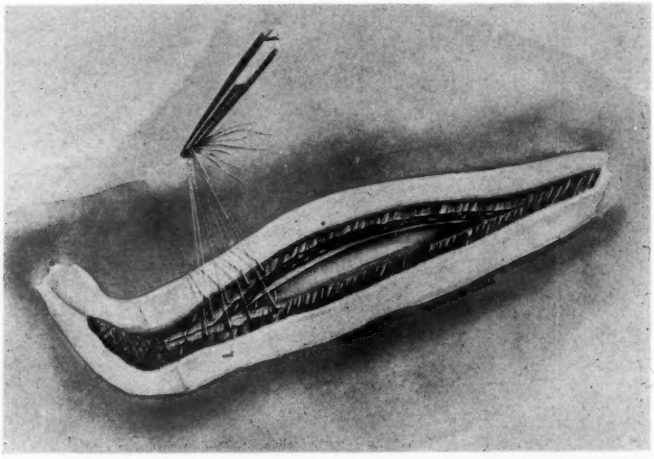


Fig. 6.—Interrupted cotton sutures are placed through the pleura and intercostal muscles 7 to 8 mm. apart.

RESULTS

In our series of 109 consecutive cases, in which intercostal incision was planned, it has not been necessary to resect a rib or portion of rib. In five of the earlier cases, anterior division of the rib was resorted to because of miscalculation in selecting the proper interspace, and anterior section was made through the cartilage. In four cases in which a rib was fractured during the spreading of the ribs, postoperative intercostal pain persisted for five to nine days in three cases and was moderately severe for several months in the third case. In three instances a rib was dislocated from the sternum but caused no postoperative discomfort.

The ages varied from 20 to 69 years, with the following distribution: 27.4 per cent between 20 and 29 years, 31.3 per cent between 30 and 39 years, 14.7 per cent between 40 and 49 years, 23.6 per cent between 50 and 59 years, and 3 per cent between 60 and 69 years.

In the older patients in whom the intercostal approach was used, no difficulties were encountered in obtaining satisfactory exposure.

Sweet[4] suggested that the chest wall is inflexible in the middle and older age patient, and therefore preferred resection of a rib to intercostal incision in the supradiaphragmatic approach in the repair of a hiatus hernia. In our experience there did not appear to be any appreciable difference in the exposure obtained among the various age groups.

Of the total number of cases there were sixty transthoracic vagotomies. There were three patients in whom the rib was divided at the anterior margin and three patients (ages 32, 34, and 41 years) in whom a rib was fractured near the vertebral border in spreading the ribs. X-ray evidence of pneumonitis occurred in four with clinical symptoms and signs in only one of these; all subsided on antibiotic therapy. Pleural effusion occurred in eight cases. Of these, three were moderately severe and occurred in the patients in whom a rib had been fractured at operation. In none of these with pleural effusion was thoracentesis performed. In one instance a severe pleural effusion occurred, followed by disruption of the wound and spontaneous drainage of 1,500 c.c. of fluid. This was the patient with the extensive pneumonitis. Intercostal pain occurred in nine patients; in six the pain was slight and present for one to two days. In two patients the pain was present for seven and nine days and in one patient the pain persisted for three months postoperatively. This occurred in the patients in whom a rib was fractured at operation.

Dragstedt and Owens[5] originally described rib resection for transthoracic vagotomy. In our experience exposure has been very satisfactory using the intercostal approach.

Transdiaphragmatic splenectomy was performed in three cases. There were no instances of either pneumonitis or atelectasis. Pleural effusion occurred to a slight degree in one patient and was moderate in another. None complained of intercostal pain.

Repain of diaphragmatic hernia through the intercostal approach was done in six cases. There was x-ray evidence of pneumonitis in one patient. Pleural effusion was slight in three patients, none of whom required thoracentesis. One patient complained of pain in the incision and this was for only three days postoperatively.

Exploratory thoracotomy using an intercostal incision was performed on six patients. In one, pleural effusion occurred to a slight degree. There were no instances of pneumonitis, atelectasis, or intercostal pain.

Seven pneumonectomies were done without resection or division of the ribs. Pneumonitis occurred in one. Intercostal pain was slight in two of the patients, lasting for two days in one and for four days in the other, and severe in the patient in whom a rib had been fractured. Pleural effusion occurred in all cases. This was also true of other operative procedures in which there was extensive surgery involving the lung.

There were seven patients on whom either lobectomy or segmental resection of a lobe was performed. Pleural effusion occurred in all instances and was

severe in five. Intercostal pain was complained of by one patient for the first three postoperative days.

Decortication of the lung was performed on thirteen patients without rib resection. All had pleural effusion. None complained of intercostal pain or showed evidence of pneumonitis or atelectasis.

Intercostal drainage was performed in four cases of pleural empyema and in one case of pericardial empyema. There were no instances of pneumonitis, atelectasis, or intercostal pain.

Our experience with gastric resection through an intercostal approach is limited to two cases. However, the excellent exposure obtained through a more than adequate incision, with a minimum of postoperative complications warrants continued use of this approach.

DISCUSSION

The use of the intercostal incision is as old as surgery of the thorax, but with few exceptions the procedure has not been given special attention. Walton[6] related that, in 1882, he met a Doctor Block who was exhibiting specimens of intrathoracic surgery in Prof. Virchow's laboratory. The specimens shown were limited to rabbits, but the doctor stated that he had shown that in cows, swine, and dogs, as well as in rabbits, the various lobes of the lungs could be removed quickly (three minutes), easily, and safely through incisions in the intercostal spaces without cutting ribs or costal cartilages, and was so confident that similar operations could be performed successfully on man, that he declared himself ready to operate at the earliest opportunity.

Roux,[7] in treating empyema, made an incision in the intercostal space anteroinferiorly in an attempt to preserve as much of the bony thoracic wall as possible. Lilienthal,[8] in 1926, described a long intercostal incision and the use of rib spreaders both with and without sectioning ribs.

Rienhoff[9, 10] described the use of an intercostal incision in pneumonectomy in 1933, and in 1947, reported a series of 112 pneumonectomies in which anterior intercostal incision was used.

Shenstone,[11] in reporting eighteen cases of pneumonectomy, used a posterolateral incision with the fifth or sixth interspace as the portal of entry in sixteen of the cases, and was of the opinion that this approach gave better access to all of the structures about the lung than the anterior approach.

Johnson[12] reported that postoperative pain was severe in twenty cases of pneumonectomy in which an anterolateral incision in the fifth interspace was used and therefore recommended crushing the second to seventh intercostal nerves.

Samson and Burford[13] and Burford, Parker, and Samson,[14] in describing their technique of pulmonary decortication, prefer an intercostal incision without section or resection of ribs. However, they inject two or three nerves above and below the incision with 1 per cent procaine.

A comparison was made in thirty of our early cases by injecting the intercostal nerves above and below the incision in alternate cases. Pain did not occur in either of the two groups and it was obvious that injection of the nerves was unnecessary.

Others have described intercostal approach in operative procedures on the esophagus. Clark and Adams[15] obtained excellent exposure by an eighth intercostal space incision for esophagogastrostomy. Janes[16] used a posterolateral approach through the seventh or eighth interspace in four cases for operation of diverticulum of the lower thoracic esophagus. Ochsner and DeBakey[17] suggested as one of the approaches, a long intercostal incision for exposure in the resection of a carcinoma of the esophagus.

Blakemore[18] described the use of an intercostal incision using the right eighth interspace in the transdiaphragmatic approach in porto-caval shunts and was of the opinion that it affords excellent exposure for anastomosing the portal vein to the vena cava.

TABLE I

	TOTAL CASES	PNEUMONITIS	ATELECTASIS	PLEURAL EFFUSION		INTERCOSTAL PAIN	
				MILD	MODERATELY SEVERE	MILD	SEVERE
Transthoracic vagotomy	60	4	0	4	4	6	3
Transdiaphragmatic splenectomy	3	0	0	1	1	0	0
Repair of diaphragmatic hernia	6	1	0	3	0	1	0
Exploratory thoracotomy	6	0	0	1	0	0	0
Pneumonectomy	7	1	0	0	6	2	1
Lobectomy and segmental resection	7	0	0	2	5	1	0
Decortication	13	0	0	0	13	0	0
Drainage of pleural and pericardial empyema	5	0	0	-	-	0	0
Gastric resection	2	0	0	1	0	0	0

SUMMARY

The postoperative morbidity following thoracotomy with intercostal incision as compared with costal resection or posterior costal section has been studied at the Birmingham Veterans Administration Hospital. The intercostal incision has been used routinely in a consecutive series of 109 cases including pneumonectomy, lobectomy, segmental pulmonary resection, pulmonary decortication, drainage of acute and chronic pleural empyema, pericardiotomy, transthoracic vagotomy, transdiaphragmatic splenectomy, repair of diaphragmatic hernia, and subtotal gastrectomy.

Adequate exposure has been attained in all transpleural procedures since its routine use was adopted. In several cases in which the proper lever of intercostal incision was miscalculated, division of a costal cartilage was resorted to, but in no instance has it been necessary to resect a rib or divide a rib posteriorly.

The intercostal approach has more advantages than the obvious ones of facilitation of wound closure and maintenance of the normal contour of the thoracic wall. Its routine use has practically eliminated the distressing symptom of intercostal neurodynia. Also, a comparison with earlier cases operated on in which resection or posterior division of a rib was performed, reveals a lower incidence of postoperative pleural effusion, atelectasis, and pneumonitis.

The technique of operation and the levels of incision for the various transpleural procedures are described.

ADDENDUM

Since this paper was submitted there have been 72 operations with intercostal incision, including 10 pneumonectomies, 17 lobectomies, and 18 total pleural decortications. The average age of this additional group is higher than that in the cases described in the body of the report. There has been a higher incidence of fracture of the ribs, approximately 10 per cent, which is probably explained by the older age of the patients. However, fracture has not added materially to the incidence of intercostal pain.

REFERENCES

1. Grimson, K. S.: Complications of Thoracotomy Observed During Operations Upon Sympathetic and Vagus Nerves, S. Clin. North America **26:** 1108-1123, 1946.
2. Bailey, C. P.: Lung Resection for Pulmonary Tuberculosis, J. THORACIC SURG. **16:** 328-341, 1947.
3. Graham, E.: Influence of Respiratory Movements on the Formation of Pleural Exudates, J. A. M. A. **12:** 784-785, 1921.
4. Sweet, R. H.: The Repair of Hiatus Hernia of the Diaphragm by the Supradiaphragmatic Approach, New England, J. Med. **19:** 649-653, 1948.
5. Dragstedt, L. R., and Owens, F. M., Jr.: Supradiaphragmatic Section of Vagus Nerves in Treatment of Duodenal Ulcer, Proc. Soc. Exper. Biol. & Med. **53:** 152-154, 1943.
6. Walton, G. L.: Letter From Berlin. Resection of the Lung as Proposed by Dr. Block, Boston M. & S. J. **108:** 261, 1883.
7. Roux: Quoted in Violet: De la décortication pulmonaire dans l'empyème chronique, Arch. gén. de méd. **193:** 657, 1904.
8. Lilienthal, H.: Thoracic Surgery, Vol. 2, Philadelphia, 1926, W. B. Saunders Company.
9. Rienhoff, W. F., Jr.: Pneumonectomy, Bull. Johns Hopkins Hosp. **53:** 390, 1933.
10. Rienhoff, W. F., Jr.: The Present Status of the Surgical Treatment of Carcinoma of the Lung, Ann. Surg. **5:** 541-564, 1947.
11. Shenstone, N. S.: Experiences With Total Pneumonectomy, J. THORACIC SURG. **4:** 405-413, 1942.
12. Johnson, J.: Postoperative Pain Following Total Pneumonectomy, J. THORACIC SURG. **8:** 702-703, 1943.
13. Samson, P. C., and Burford, T. H.: Total Pulmonary Decortication, J. THORACIC SURG. **2:** 127-145, 1947.
14. Burford, T. H., Parker, E. F., and Samson, P. C.: Early Pulmonary Decortication in the Treatment of Post-traumatic Empyema, Ann. Surg. **122:** 163-190, 1945.
15. Clark, D. E., and Adams, W. E.: Transthoracic Esophagogastrostomy for Benign Strictures of the Lower Esophagus, Ann. Surg. **122:** 942-953, 1945.
16. Janes, R. M.: Diverticulum of Lower Thoracic Esophagus, Ann. Surg. **124:** 637-652, 1946.
17. Ochsner, A., and DeBakey, M.: Surgical Aspects of Carcinoma of the Esophagus; Review of the Literature and Report of 4 Cases, J. THORACIC SURG. **10:** 401-445, 1941.
18. Blakemore, A. H.: Portacaval Anastomosis—Observations on Technic and Postoperative Care, S. Clin. North America **2:** 279-289, 1948.

PERICARDIAL CELOMIC CYST, WITH SYMPTOMS

A Case Report

WENDELL H. KISNER, M.D., AND JOHN C. REGANIS, M.D.
NEW ORLEANS, LA.

PERICARDIAL celomic cysts are not common, and it is still more rare for them to produce symptoms. The following case is presented because there was associated discomfort. When present, the lesion is difficult to differentiate from a malignancy in the anterior mediastinum or a herniation of omentum through the space of Morgagni.

The patient was a 56-year-old white man who entered the hospital because of the known presence of a mass in the thorax discovered by his family physician. The patient had noticed a discomfort in the precordial region for the seven weeks preceding his visit to this physician. This discomfort was especially noticeable when he was fatigued. The patient stated there was no real pain in the left chest, but just an uncomfortable feeling that was difficult to describe. There was no history of cough, hemoptysis, or weight loss.

Physical examination revealed a well-developed and well-nourished white man who did not appear to be ill. The blood pressure was 114/80 and the pulse was 76 per minute. No abnormality was discovered on physical examination. The hemoglobin was 92 per cent; red blood cells, 4.97; white blood cells, 6,450; Wassermann, negative; and urinalysis, negative.

An x-ray film of the chest revealed a large, 8 cm. diameter, well-defined mass of soft tissue density in the left cardiophrenic angle anteriorly. Instillation of Lipiodol revealed no definite obstruction or displacement of the bronchi in the neighborhood of the mass. None of the medium entered the mass. An upper gastrointestinal series showed no connection of the gastrointestinal tract with the mass in the thorax. At the end of twenty-four hours the entire large bowel was outlined. At no time was any of the gastrointestinal tract visualized above the diaphragm.

Operation was advised, but the patient postponed it until two months later, when he entered the Southern Baptist Hospital in New Orleans for exploratory thoracotomy.

Roentgenologic and fluoroscopic examination of the chest was repeated in the hospital. This examination revealed a residue of Lipiodol in the base of each lung and a sharply defined mass in the left cardiophrenic angle anteriorly. This mass had the same appearance as on previous examinations two months before. On fluoroscopic examination it could never be separated from the cardiac shadow and showed definite transmitted pulsation. On respiration the mass did not descend with the diaphragm, but showed only the same minimal excursion that the heart showed. The impression was gained that the mass was not only adjacent to the heart or pericardium, but was actually attached to it.

Operative Description.—The patient was placed in the right lateral position and under endotracheal anesthesia the greater portion of the seventh rib was resected and the pleura opened. Exploration revealed a thin-walled, multilocular cyst about 8 cm. in diameter located in the left anterior cardiophrenic angle. This mass was dissected from the pericardium medially and the diaphragm inferiorly. There was little bleeding and no ligatures were necessary. No other abnormality was present. The chest was closed in the usual manner after reinflating the lung. The postoperative course was uneventful. An electrocardiogram taken postoperatively was within normal limits.

Follow-up examination two months later revealed the patient to be in excellent health and free of the precordial discomfort.

From the Mahorner Surgical Group.
Received for publication May 23, 1949.

Pathologic Report.—Gross description: The pericardial cyst consisted of a clear wall multilocular cyst measuring 8 cm. in diameter. The walls were thin and the blood vessels prominent. There was a small amount of fat around the periphery.

Microscopic description: Section through the wall of the cystic cavity showed the lining to consist of endothelial cells which in some areas were elongated and flattened. In others they were two to three cell layers deep and here assumed a more cuboidal appearance. Their nuclei were round to oval, deeply stained, and adult in age. The amount of cytoplasm was moderate with light pink staining characteristics. The underlying tissue consisted of edematous connective tissue and varying amounts of fat. The small capillaries were adult in age and congested. The cyst cavity was irregular in outline and showed small protrusions from the surface into the lumen of the cavity forming small papillary projections. These consisted of a stalk of fat and fibrous tissue covered with the same type of endothelial cells as described for the major portion of the cyst.

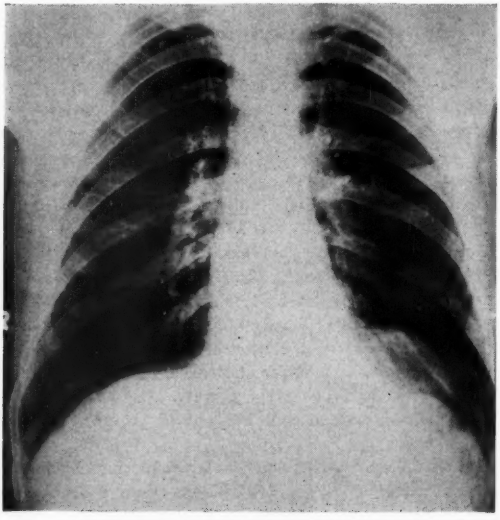


Fig. 1.—Preoperative roentgenogram of chest.

DISCUSSION

Pericardial cysts are usually discovered on routine x-ray examination of the chest. The patient reported here was disturbed by an uncomfortable feeling in the left chest and consulted his family physician.

PATHOLOGY

Lambert[1] attributed the origin of pericardial cysts to failure of primitive mesenchymal lacunae which form the pericardium to fuse with others and instead form independent cavities. Failure of fusion of these lacunae may result in other anomalies such as congenital absence of the pericardium, congenital diverticulum of the pericardium, or congenital hernia of the diaphragm.

Lambert[1] proposed the name, pericardial celomic cysts, as being a more accurate term to define their true character. Lambert[1] also reported two cases of pericardial celomic cyst in his paper.

According to Thompson,[2] Freedlander and Gebauer suggested that pericardial defects might be produced by failure of fusion of the embryonic transverse septum with the pleuropericardial or pleuroperitoneal membranes.

Laipply[3] is in accord with Lambert[1] in reference to the origin of pericardial cysts.

INCIDENCE

These lesions are not common and are usually found on routine x-ray examinations of the chest. Out of a large series of cysts and cystic tumors of the mediastinum Laipply[3] found only four pericardial celomic cysts. Blades,[4] in a series of 109 cases of mediastinal tumors, found ten pericardial celomic cysts. The higher incidence of these cysts in Blades' series is probably a result of the large number of routine roentgenograms of army personnel. All of the pericardial cysts in his series were asymptomatic. Lam,[5] in 1947, and others have reported single cases of pericardial celomic cysts.

PATHOLOGY

Pathologically the reported cases of pericardial cysts are similar to the case herein reported. The walls of the cysts are made up of fibrous connective tissue lined by a layer of flattened endothelial or mesothelial cells. Blades[4] is of the opinion that in the past some of these cysts may have been classified as cystic hygromas or cystic lymphangiomas.

Pericardial celomic cysts are found in the anterior mediastinum in contact with the anterior thoracic wall, the parietal pericardium, and sometimes the diaphragm and the lung.

SYMPTOMS

Pericardial cysts rarely cause symptoms. Pickhardt[6] reported a case of pleurodiaphragmatic cyst in 1934. This patient was a 53-year-old woman who complained of sharp, knifelike pain over the precordium for a period of several weeks. The case herein reported and Pickhardt's case are the only two in the literature in which symptoms were attributed to a pericardial cyst. Both patients were relieved by removal of the cyst.

DIAGNOSIS

In an attempt to establish the diagnosis of pericardial cyst, bronchiogenic carcinoma, diaphragmatic hernia through the space of Morgagni, and dermoid tumor are the lesions most likely to be confused with benign cyst.

The history of cough is suggestive of bronchiogenic carcinoma. Careful roentgenologic studies with instillation of Lipiodol in the bronchial tree, bronchoscopy, and histologic study of cells aspirated through the bronchoscope will aid in making a positive diagnosis of carcinoma.

Herniation of omentum through the space of Morgagni can be confusing in the differential diagnosis. An upper gastrointestinal series should be done in all of these patients in order to rule out the presence of herniated stomach or

bowel through the diaphragm. Careful fluoroscopic examination is the most important means of differentiating a diaphragmatic hernia from a pericardial cyst.

A dermoid tumor or teratoma in the anterior mediastinum is best differentiated from a pericardial cyst by fluoroscopic examination.

Careful physical examination should be done in order to rule out the possibility of a solitary metastasis to the lung.

In summation, the final diagnosis of pericardial cyst, even though suspected, is usually made by exploratory thoracotomy.

TREATMENT

The treatment of pericardial celomic cyst is surgical removal. In spite of the fact that these lesions are benign and rarely cause symptoms, exploratory thoracotomy should be carried out because of the possibility of malignancy being present. This procedure today carries so little risk these patients should be urged to undergo surgery.

The actual removal of the cyst is not a difficult procedure, as the lesion is easily dissected from the pericardium and the diaphragmatic pleura with little loss of blood.

SUMMARY

A case of pericardial celomic cyst is presented. This case and the case reported by Pickhardt[6] are the only two cases of pericardial celomic cyst reported in the literature in which the symptoms were attributed to the cyst. The symptoms in both cases were relieved by removal of the cyst.

CONCLUSION

Pericardial celomic cysts, even though benign, should be removed. The difficulty of ruling out the presence of a malignancy makes exploratory thoracotomy imperative.

REFERENCES

1. Lambert, A. V. S.: Etiology of Thin Walled Thoracic Cysts, J. THORAC. SURG. **10**: 1-7, 1940.
2. Thompson, J. V.: Mediastinal Tumors and Cysts, Internat. Abstr. Surg. **84**: 195-221, 1947.
3. Laipply, T. C.: Cysts and Cystic Tumors of the Mediastinum, Arch. Path. **39**: 153-161, 1945.
4. Blades, B.: Mediastinal Tumors, Ann. Surg. **123**: 749-765, 1946.
5. Lam, C.: Pericardial Coelomic Cysts, Radiology **48**: 239-243, 1947.
6. Pickhardt, O. C.: Pleurodiaphragmatic Cyst, Ann. Surg. **99**: 814-816, 1934.

PLEURAL MESOTHELIOMA

Further Evidence of Its Histogenesis

Machteld E. Sano, M.D., Edward Weiss, M.D., and Edwin S. Gault, M.D.
Philadelphia, Pa.

MORE and more evidence has accumulated in the last ten years to support the concept of the histogenesis of pleural mesothelioma. The studies in tissue culture of such a tumor by Stout and Murray[1] have been one of the outstanding contributions on the subject in the last decade. However, there are still those[2, 3] who dispute the pleural origin of any of these tumors and believe they are not primary tumors of the lining cells, but represent metastatic lesions. Others[19] feel there is insufficient evidence as yet to settle the question. No record of new experimental data to substantiate the concept of the mesothelioma could be found in the literature since 1942, and for this reason we present the clinical, histologic, and tissue culture findings in this case.

The basic reason for the controversy is more easily understood when it is realized that often histologic examination alone does not reveal the immediate potentialities of cells in general and of mesothelial lining cells in particular. Lewis[4] has shown by tissue culture that the mesothelium lining the serous cavities is not highly differentiated and may assume different forms. If this is true, greater lability of the cells of the mesothelium can be expected under the influence of varied conditions of environment, or the pleura by its very location is exposed to many physical and physicochemical stimuli. Its smooth surface serves as ideal support for cell proliferation, without tissue barriers. The lung, on the other hand, an actively functioning structure, offers mechanical resistance as well as producing physicochemical influences,[5] and thus encouraging surface spread of the tumor. Last but not least, the physicochemical individuality of the host may influence the growth of the tumor, as will be demonstrated. These may therefore be determining factors in the physiognomy of the growth with resulting difficulty in diagnosis. The mesothelial cells may grow in membranes, or they may assume a more epithelial-like form, as a result of irritation.[6, 7, 8] In inflammation they can become elongated and spindled like fibroblasts.[9] It is therefore not surprising that tumors of the pleural mesothelium assume either the gamut of these variations or retain one of these forms only. It is of particular significance that these particular patterns are not found in metastatic carcinoma.

It is now generally accepted that there are two types of tumors:[10] the diffuse, rapidly spreading kind which has both a fibrosarcomatous appearance and epithelial-like cells, and the localized, fibrosarcomatous, slowly growing tumor. In the latter the epithelial-like element is never present, in the former it is usually present, but in rare instances may be absent, which leads us to the tumor under observation.

From the Temple University Medical School and Hospital.

Research supported by the Agnes Barr Chase Cancer Research Foundation, Temple University Medical School and Hospital.

Received for publication May 25, 1949.

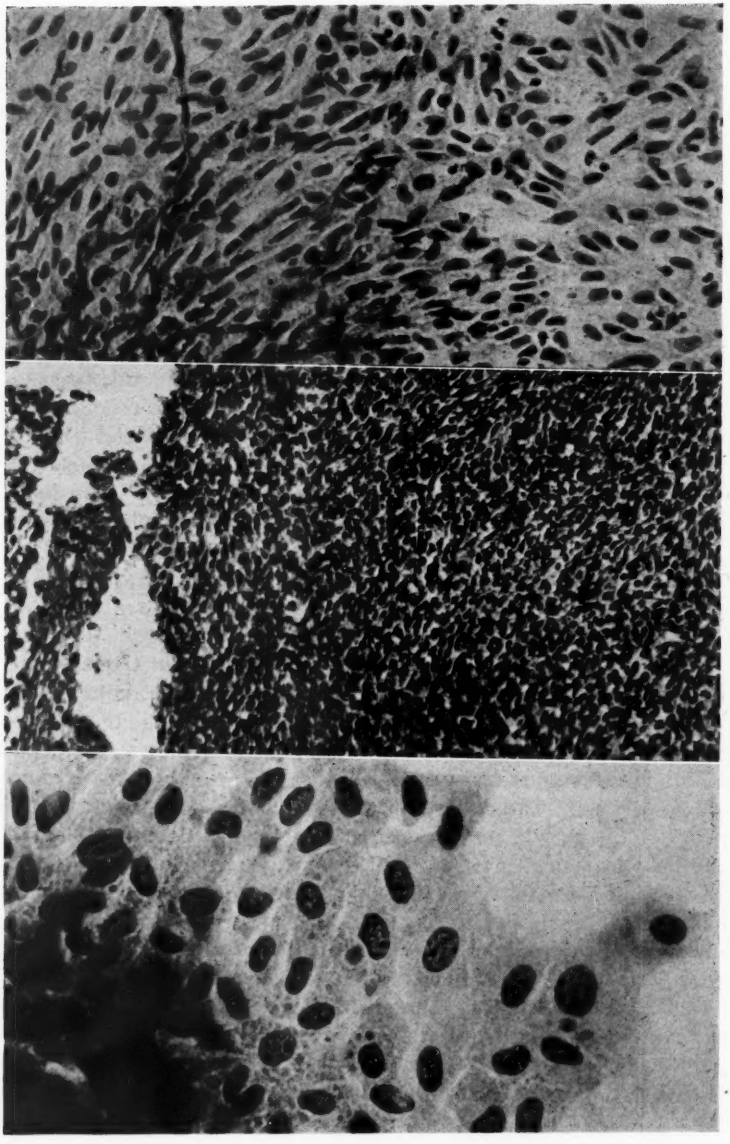


Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1.—Tissue culture showing the spindling of the cells. Stain CR 304, (18) (×200).
Fig. 2.—Section of the tumor. Stain CR 304 (×200).
Fig. 3.—Note the flattened cells growing out in sheets in tissue culture. Stain CR 304 (×400).

CASE HISTORY

The patient, a 57-year-old, well-developed, well-nourished man fell through a manhole in September, 1948, injuring the right thorax, with subsequent sharp pains in the right chest and upper abdomen and slight cough. Roentgenograms of the chest at the time were negative, but he continued to have vague pains. He was admitted to the hospital on Feb. 1, 1949, and presented fluid in the right chest. General condition was excellent, though for the previous three weeks there had been marked loss of appetite. Bronchoscopy showed compression of

Fig. 4.

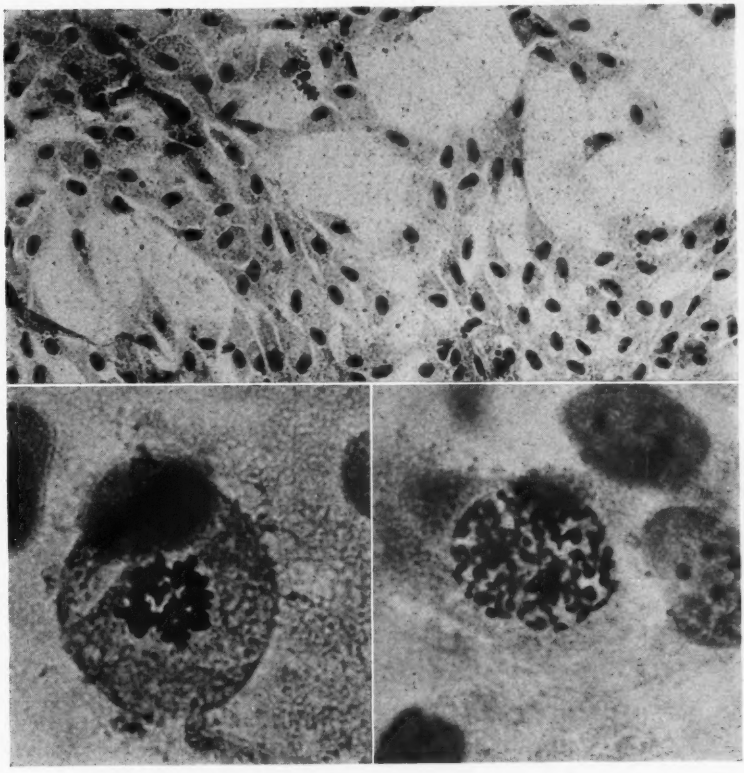


Fig. 5. Fig. 6.

Fig. 4.—The tendency to alveolar arrangement in tissue culture is here demonstrated. Stain CR 304 (×200).
Fig. 5.—Fairly well-balanced mitosis in tissue culture. Stain CR 304 (×1400).
Fig. 6.—Multipolar mitosis in tissue culture. CR 304 (×1400).

the right main bronchus, but there were no mucosal lesions. An exploratory operation was done,* but the pleura was completely involved, as was the pericardium. Careful examination and multiple sections at post-mortem† revealed this tumor to be grossly and microscopically a mesothelioma with none of the epithelial-like elements present. No tumors were located elsewhere, notwithstanding multiple sections. Was this, therefore, originally a well-localized operable tumor as its histology would suggest, or a diffuse type, as one would surmise from the clinical history?

*By Dr. W. E. Burnett and Dr. G. Rosemond.
†By Dr. Paul S. Guerin, Resident in the Department of Pathology.

Behavior of the Tumor in Tissue Culture.—Fragments of necrotizing tumor and firm tumor nodules were taken at the time of operation. These were inoculated into two types of media: Tyrode's solution, 1 part; mouse embryo extract, 1 part; and autogenous human plasma, 1 part. In the other medium, chicken plasma was substituted for human plasma.[11, 12]

Fig. 7.

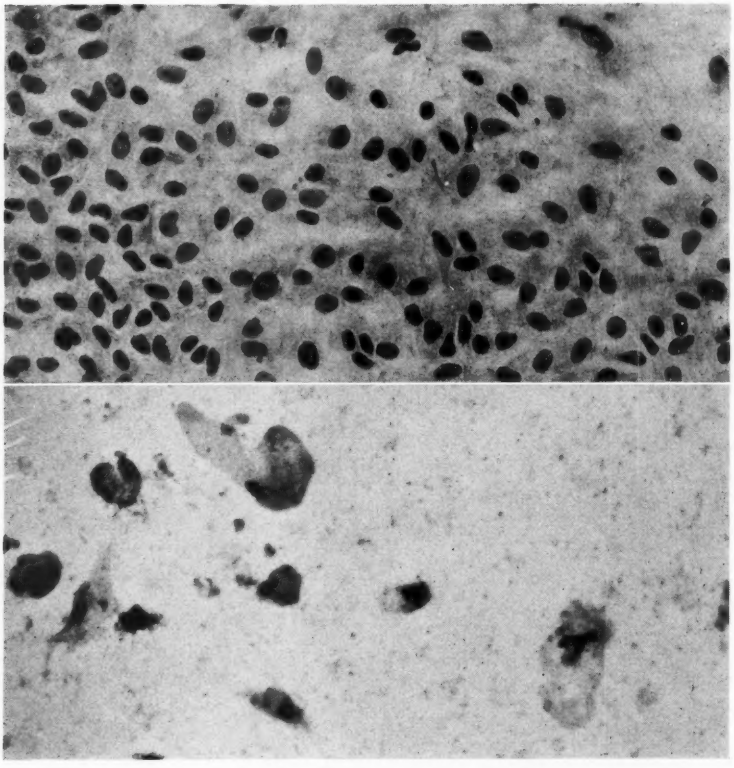


Fig. 8.

Fig. 7.—Tissue culture of tumor in medium containing chicken plasma. Stain CR 304 (×200).

Fig. 8.—Bizarre forms of isolated cells near periphery of growth in tissue culture in chicken plasma medium. Stain CR 304 (×1400).

There were two outstanding characteristics common to the growth in either media. One was the rapidity of growth which was profuse within twenty-four hours. The other was that, from minute particles of seemingly nonviable tissues containing three to four pienotic nuclei, tumor cells proliferated within forty-eight hours, reproducing rapidly. In the human plasma the fixed cells growing out from the thicker fragments were at first more spindle shaped (Fig. 1), similar in appearance to the arrangement in the section of the tumor (Fig. 2). As the cells became less crowded, they flattened out, growing in membranes. They had a mosaic arrangement (Fig. 3), which was very characteristic and emphasized by phase illumination. Under this light, an accumulation of fine mitochondria in the cytoplasm and surrounding the nucleus could be seen. The outlines of the unstained cells were almost invisible unless examined under reflected light. The layers closest to the glass coverslip grew most rapidly.

Where growth was unusually rapid, the cytoplasm was extremely light and delicate. The intercellular boundaries were usually well marked. The cells had a plump oval nucleus with fine to medium heavy metachromatic threads and two or more nucleoli.

In some of the smaller fragments the cells grew out in sheets at first, then while still flattened (in form) they tended to form alveoli which were not secondary to fibrinolysis (Fig. 4). There was in fact, very little liquefaction even over a period of eighteen days. Syneresis was marked in the human plasma, but that is a common occurrence within the first twelve hours.

The mitoses in the cells were as often balanced as unbalanced. In the unbalanced form there was remarkably little change in the shape of cells (Figs. 5 and 6). Normal wandering cells were few and rare in both media, the growth being formed mainly by tumor cells.

The growth in the chicken plasma was different. Some of the cells grew in sheets (Fig. 7), but as the new growth became about three cells deep, the cells took on a rounder form with the nuclei placed near the periphery. These cells isolated themselves. Their outline was irregular and they had a tendency to assume bizarre forms (Fig. 8) with numerous atypical mitoses. These cells did not resemble any of the cells seen in the original tumor masses, but were very similar in character to the epithelial-like cells seen in the usually rapidly spreading tumor of the pleura. None of these cells were found in any of the multiple sections taken of the tumor post mortem.

Once again we observed, therefore, as one of us[12] has noted on numerous occasions in the study of human tumors and lymph nodes for the past ten years, that the form a tumor assumes in the host is in part, at least, dependent on a factor present in the host, besides the purely physical environmental factors. This elusive factor can usually be demonstrated in the plasma of the host. Many workers have observed the difference between human plasma of cancer patients and of normal individuals. There is a difference in the coagulation,[13] frequently a difference in pH reading,[14, 15] a difference in the plasma pattern,[16] and in its reducing power.[17] Some of these observations have been verified, others have been contradicted, yet, there is some truth in most of them, though none of them as yet stand up as reliable cancer tests. Whether this is one and the same factor or a different one has not been verified because the observations under present techniques are still too inconstant.

DISCUSSION

In the pleural tumor under consideration only the spindle form of cell was apparent, but under the different conditions created by tissue culture, the epithelial-like form was demonstrated as well. Clinically, moreover, the diffuse and rapid growth resembles the behavior of the mixed form of pleural mesothelioma, further emphasizing the importance of the tissue culture findings.

One of the determinants of the dominant cell types is evidently present in part in the plasma of the tumor host. Whether it is a reaction of the host to the tumor or whether it is a physicochemical property in the plasma or tissues of the host which precedes tumor development, we were unable to demonstrate. We do know from experience that when tissue culture is used as a diagnostic aid in atypical tumors, it is always advisable to use the autogenous plasma, in addition to the standard chicken plasma. Actual and potential forms of tumors can thus not infrequently be demonstrated.

In reviewing the literature we have been impressed by the resemblance of the tissue culture of this tumor with that of the pleural mesothelioma studied by Stout and Murray. It further emphasizes the value of this method in the study of unusual tumors and the consistency of growth in tissue cultures of similar tumors.

RÉSUMÉ AND CONCLUSIONS

1. Report of a case of pleural mesothelioma with rapid diffuse spread is presented.

2. The histopathologic characteristics seen are those of the fibrosarcomatous slow-growing type, and therefore operable.

3. Tissue culture in autogenous plasma reveals the mesothelial character of the cells.

4. Tissue culture in chicken plasma reveals the potential epithelial-like cell form, placing it in the rapidly spreading group, usually inoperable.

5. Discussion of the factors influencing the form of the mesothelial cell is presented.

Note.—We are indebted to Carol Bocher, B.S., for valuable technical assistance.

REFERENCES

1. Stout, A. P., and Murray, Margaret, R.: Localized Pleural Mesothelioma. Investigation of Its Characteristics and Histogenesis by the Method of Tissue Culture, Arch. Path. **34**: 951-964, 1942.
2. Robertson, H. E.: Endothelioma of the Pleura, J. Cancer Research **8**: 317-375, 1924.
3. Willis, R. A.: Metastatic Deposit of Bronchial Carcinoma in Hydrocele Misdiagnosed "Endothelioma" With Review of Supposed "Endothelioma" of Serous Membranes, J. Path. & Bact. **47**: 35-42, 1938.
4. Lewis, W. H.: Mesenchyme and Mesothelium, J. Exper. Med. **38**: 257-261, 1923.
5. Holtfreter, J.: Concepts on the Mechanism of Embryonic Induction and Its Relation to Pathogenesis and Malignancy, Symposia of the Society of Experimental Biology No. 2, New York, 1948, Academic Press, Inc., pp. 17-46.
6. Young, J. S.: The Experimental Production of Metaplasia and Hyperplasia in the Serosal Endothelium, and of Hyperplasia in the Alveolar Epithelium of the Lungs of the Rabbit, J. Path. & Bact. **31**: 265-275, 1928.
7. Fischer, B.: Ueber Experimentelle Erzeugung Grosser Flimmer Epithelblasen der Lunge, Frankfurt. Ztschr. f. Path. **27**: 98-184, 1922.
8. Fischer, B.: Ueber Experimentelle Erzeugung von Epithelwucherungen und Epithelmetaplasie, Verhandl. d. deutsch. path. Gesellsch. **10**: 20, 1906.
9. Maximow, A. A.: A Textbook of Histology, Philadelphia, 1948, W. B. Saunders Company, pp. 38.
10. Hochberg, L. A., Epstein, I. G., and Pernikoff, M.: Endothelioma (Mesothelioma) of Pleura, Dis. Chest **13**: 621-626, 1947.
11. Sano, M. E., and Smith, L. D.: Tissue Culture as a Diagnostic Aid in the Identification of Atypical Tumors, Arch. Path. **30**: 504-508, 1940.
12. Sano, M. E.: Cancer. (In press.)
13. Huggins, C., Miller, M. G., and Jensen, E. V.: Thermal Coagulation of Serum Proteins. II. Deficient Coagulation in Cancer and the Iodoacetate Index, Cancer Research **9**: 177-182, 1949.
14. Slosse, A.: See Reding.[15]
15. Reding, R.: Le terrain cancéreux et cancérisable, Paris, 1932, Masson & Cie.
16. Sano, M. E.: Unpublished personal observations.
17. Weiss, Emil: Color Reactions With Malignant Sera. Paper Given at the 40th Annual Meeting of The American Association for Cancer Research, April 16, 1949.
18. Sano, M. E.: Trichome Stain for Tissue Section, Culture or Smear, Am. J. Clin. Path. **19**: 898, 1949.
19. Gunn, Frances D.: In Anderson, W. A. D.: Pathology, St. Louis, 1948, The C. V. Mosby Company, pp. 748.

ARTERIOVENOUS FISTULA OF THE LUNG

With Report of a Case

James Carswell, Jr., M.D.*
McKinney, Texas

SINCE 1942, when Hepburn and Dauphinee[9] reported a case of hemangioma of the lung diagnosed clinically and successfully treated by pneumonectomy, an increasing number of reports of pulmonary arteriovenous fistula has appeared in the literature. These authors reviewed the literature prior to their paper and found few references describing the occurrence of this lesion. Janes,[10] in 1944, reported the first case of multiple cavernous hemangioma of the lungs successfully treated by local resection of the tumors. Since the lesions were bilateral, treatment was carried out in two stages, approximately eight months apart. Maier and associates,[13] in 1948, presented a study of the circulatory dynamics in pulmonary arteriovenous fistula and included a case of their own complicated by bacterial endarteritis and successfully treated by chemotherapy and lobectomy. In the discussion of Maier's paper, several other cases of arteriovenous fistula of the lung were brought to light. Wodehouse,[18] in 1924, added two cases previously unreported, one of which was complicated by a brain abscess. Additional reports[1, 2, 3, 5, 7, 8, 11, 14, 16, 17] bring the total number of cases in the literature to twenty-eight.

It is likely, as Wodehouse implied, that the earlier reports have resulted in an increased awareness of arteriovenous fistula of the lung as a clinical entity. The signs and symptoms, although variable[13] should arouse suspicion of such a lesion. Those most frequently mentioned in the reported cases were cyanosis, polycythemia, clubbing of the extremities, and the appearance of a pulmonary density by x-ray examination. An audible murmur over the lesion and expansile pulsation of the mass fluoroscopically are inconstant findings. Dyspnea,[9, 12] hemoptysis,[5, 6] and the occurrence of coexisting hemangiomas elsewhere in the body may appear as prominent symptoms in some cases of arteriovenous fistula.[4, 13, 15]

CASE REPORT

Illness at Time of Admission.—A 20-year-old delivery-truck driver was admitted to this hospital February 23, 1948, because of recurrent mild, shooting pains in the interscapular region, of two years' duration. The pain usually lasted several minutes, recurring at irregular intervals of a few days to weeks, and was not incapacitating. It was unrelated to exercise, emotional excitement, or the ingestion of food, and was not initiated or aggravated by deep breathing. There had been no cough, dyspnea, hemoptysis, weight loss, or loss of appetite. In April, 1946, one month after the onset, a chest roentgenogram revealed a small, circumscribed area of increased density in the posterolateral aspect of the right lower lobe. In May, 1946, a bronchogram was done but contributed no further information. Bronchoscopy in November, 1947, was negative. The patient was referred to this hospital for further study and exploratory thoracotomy.

Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the author are the result of his own study and do not necessarily reflect the opinion or policy of the Veterans Administration.
Received for publication June 9, 1949.

*Chief of Thoracic Surgery Section, Veterans Administration Hospital.

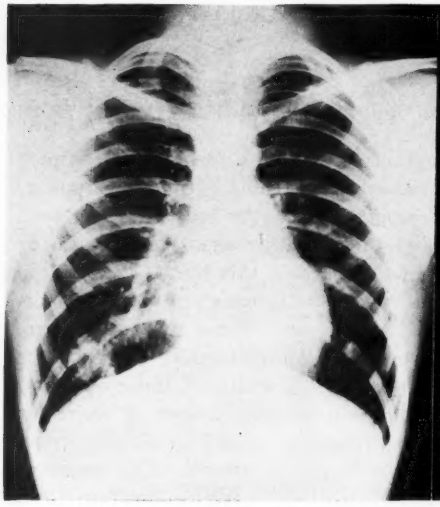


Fig. 1.

Fig. 2.

Fig. 1.—Posteroanterior view showing lesion in the right base.
Fig. 2.—Right lateral view showing lesion in the posterior basilar segment of the right lower lobe.

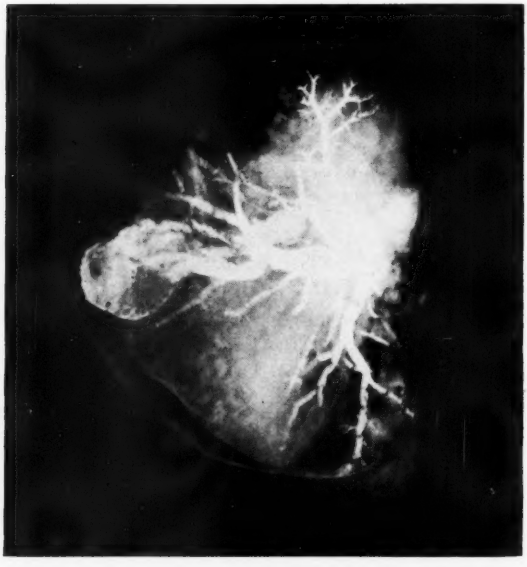


Fig. 3.—Superior-inferior view of the inflated, injected specimen, showing the relationship of the lesion to the pulmonary vessels.

Family History.—Father had tuberculosis but the patient had not seen him for eleven years. An aunt died of cancer of the stomach at the age of 67 years. There was no history of diabetes.

Past History.—Patient stated he had been perfectly well prior to the onset of the present illness. He had had the usual childhood diseases. Tonsillectomy was done in childhood. There was no history of pulmonary infections or trauma. The patient did not use alcohol, tobacco, or drugs.

Physical Examination.—The patient was a well-developed and nourished white man who showed no signs of acute or chronic illness. Blood pressure was 130/80, pulse 78, respiration 16. Except for mild clubbing of the fingers with definite broadening of the nails, the physical examination was entirely negative. The chest was clear to auscultation and percussion and no murmur could be heard over the chest.

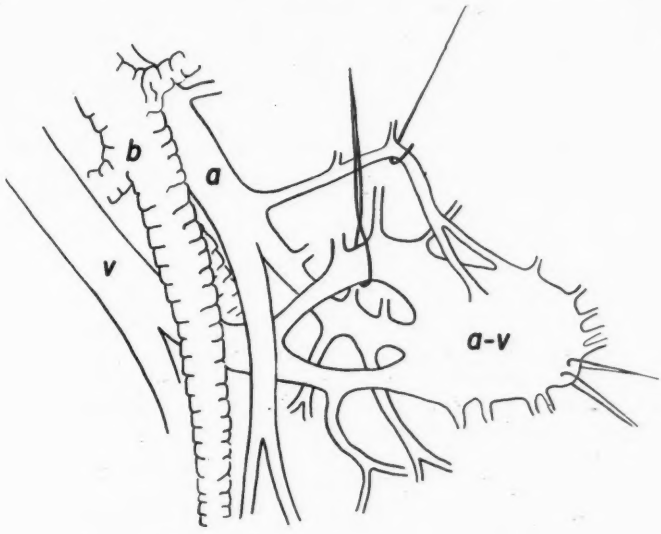


Fig. 4.—Sketch of dissection showing arteriovenous fistula.

X-ray Examination.—Roentgenogram of the chest revealed a fairly well circumscribed soft tissue density, measuring 3 by 4 cm., in the posterior basilar segment of the right lower lobe. There was a narrow stalklike density extending medially and anteriorly from this mass and merging with the hilar shadow (Figs. 1 and 2). There was no evidence of pulsation of the mass on fluoroscopy. The remainder of the lung field was clear.

Laboratory Findings.—Serology was negative; red blood count 5.85; hemoglobin 17.5 Gm.; white blood count 6.6, with a normal differential. Hematocrit was not done. Electrocardiogram was interpreted as within normal limits. Urinalysis was negative.

Hospital Course.—The patient was completely asymptomatic throughout his earlier stay in the hospital. Bronchoscopy on March 1 was negative. Bilateral bronchography March 4

gave no additional information. The patient produced no sputum, so bacteriologic studies were not done. The appearance and behavior of the lesion in the lungs, mild polycythemia, and clubbing of the fingers suggested the diagnosis of a vascular tumor, and it was decided to explore the chest.

Operation.—Thoracotomy was performed March 9 and the pleural space was found to be free of adhesions. There was a visible pulsating mass about 4 cm. in diameter immediately beneath the pleura in the inferior posterolateral aspect of the lower lobe. The thinness and transparency of the pleural covering made it possible to observe the blood eddying within the tumor. The upper and middle lobes were normal to inspection and palpation. The lower lobe was removed without incident.

Subsequent Course.—The patient's convalescense was uneventful and he was discharged from the hospital on the fourteenth postoperative day.

Gross Pathology.—The specimen consisted of the right lower lobe of the lung. On the posterolateral aspect near the base there was a soft cystlike area measuring 2.5 cm. in diameter and covered with a thin, somewhat translucent pleura. The remainder of the lobe presented no gross pathologic changes. A cannula was introduced into the bronchus and the lobe inflated, after which the bronchus was tied. A second cannula was tied into the main artery and injected with radiopaque material after infusing with saline solution to remove the blood. These solutions returned freely through the open stump of the vein. Roentgenograms of the inflated, injected lobe were made in three views before dissection of the specimen was begun. The view taken from above, with the lobe resting with its base on the cassette, shows the lesion most distinctly (Fig. 3). Dissection of the fistula along with its main arterial and venous connections was carried out, and a sketch of the dissection drawn (Fig. 4). The sac itself was unilocular, thin-walled, and lined with endothelium. It contained congealed radiopaque material admixed with blood elements. There were numerous small communications, 1.0 mm. or less in diameter, opening into the lumen of the sac. The major vessels communicating with the sac were themselves grossly normal in appearance and were not appreciably dilated. The bronchial artery was not found. The total diameter of the direct, measurable arterial communication with the sac was 12 mm., while that of the venous side was 10 mm. Numerous smaller communicating channels radiated from the wall of the sac to be lost in the surrounding parenchyma. No connection with a bronchial vessel could be demonstrated.

COMMENT

The case presented here illustrates further the variety of symptoms which may be encountered in patients with arteriovenous fistula of the lung. Mild, shooting pain in the interscapular region, intermittent and transient in character, was the only symptom of which the patient complained. Very slight polycythemia and minimal clubbing of the fingers were present. Prior to admission to the hospital, chest roentgenograms were taken and the patient was suspected of having a tuberculoma, although the possibility that the lesion might be a vascular tumor was entertained. The preoperative diagnosis was of possible vascular tumor of the right lower lobe. Unfortunately, a hematocrit was not obtained prior to surgery for later comparison. Seven weeks after operation the red blood count was 5.5, hemoglobin 16.5, a slight decrease as compared with the preoperative determinations. Three days after operation the hematocrit was 53 as compared with 49 seven weeks later.

SUMMARY

1. Prior to 1942, few references to pulmonary arteriovenous fistula were found in the literature, and the disease was considered extremely rare. In the

past six years, however, twenty-eight cases have been reported and it is probable that others have been observed.

2. A case of arteriovenous fistula of the lung is reported, in a patient whose complaint of mild interscapular pains prompted the taking of a chest film.

3. The diagnosis of pulmonary arteriovenous fistula may be made without difficulty in those patients presenting themselves with one or more of a group of symptoms commonly attending this disease. In other instances the presence of a vascular lesion in the lung may remain unsuspected for years.

REFERENCES

1. Abbott, Osler: Discussion of Maier et al., J THORACIC SURG. **17**: 25, 1948.
2. Adams, W. E., Thornton, T. F., and Eichelburger, L.: Arch. Surg. **49**: 5, 1944.
3. Adams, W. E.: Discussion of Jones and Thompson, J. THORACIC SURG. **13**: 357-371, 1944.
4. Bisgard, Dewey: Discussion of Maier et al., J. THORACIC SURG. **17**: 25, 1948.
5. Boerema, I., and Brilman, R. P.: J. THORACIC SURG. **17**: 705-708, 1948.
6. Bowers, W. F.: Nebraska Med. J. **21**: 55, 1936.
7. Byron, Francis R. X.: Discussion of Maier et al., J. THORACIC SURG. **17**: 25, 1948.
8. Goldman, Alfred: J. Lab. & Clin. Med. **32**: 330, 1947.
9. Hepburn, J., and Dauphinee, J. A.: Am. J. M. Sc. **204**: 681, 1942.
10. Janes, R. M.: Brit. J. Surg. **31**: 270, 1944.
11. Janes, R. M.: Discussion of Jones and Thompson, J. THORACIC SURG. **13**: 357-371, 1944.
12. Jones, John C., and Thompson, W. Paul: J. THORACIC SURG. **13**: 357-371, 1944.
13. Maier, Herbert C., Himmelstein, A., Riley, Richard L., and Bunin, Joseph J.: J. THORACIC SURG. **17**: 13-26, 1948.
14. Samson, Paul C.: Discussion of Maier et al., J. THORACIC SURG. **17**: 23, 1948.
15. Shefts, Lawrence M.: Discussion of Maier et al., J. THORACIC SURG. **17**: 23, 1948.
16. Sweet, Richard H.: Discussion of Maier et al., J. THORACIC SURG. **17**: 23, 1948.
17. Watson, W. Law: Surgery **22**: 909-929, 1947.
18. Wodehouse, G. E.: J. THORACIC SURG. **17**: 408-415, 1948.

PLASMA CELL TUMORS OF THE MEDIASTINUM AND LUNG

Report of Two Cases

William G. Childress, M.D., Valhalla, N. Y., and
George C. Adie, M.D., New Rochelle, N. Y.

IN 1943 in a comprehensive review of the literature Hellwig[1] collected 127 cases of extramedullary plasma cell tumor, and reported a single one of his own. Gordon and Walker[2] reported a single case of plasmacytoma of the lung in 1944. They were unable at that time to find an instance of plasmacytoma of the lung such as they reported in the literature. However, they stated that Dr. F. W. Stewart had observed two instances of solitary plasmacytoma of the lung. Bross[3] found a plasma cell tumor of the mediastinum in a 54-year-old woman at necropsy, and Klose[4] observed a similar tumor of the pleura in a 61-year-old man. We have been unable to find additional reports in the literature of either pulmonary or mediastinal tumors of this type. The two following cases were found to have plasma cell tumors in these uncommon locations.

Differences of opinion have been expressed regarding the nature of these tumors. Some regard them as carcinoma, others as granulomatous lesions resulting from chronic inflammation, and others consider them benign tumors. The tumor is characterized by an abundance of plasma cells, arranged in palisades or cartwheel distribution, and varying in size and shape with a large amount of basophilic cytoplasm. The cells often contain two or more nuclei, and giant cells and Russell bodies may be present. The tumors are widely distributed, but are more often found in the upper part of the respiratory tract, in the nose, nasopharynx, mouth, and tonsils. Other sites are stomach, intestines, thyroid gland, kidney, ovary, skin, lymph nodes, and spermatic cord.

Case 1.—M. R., a 37-year-old white male laundry worker, was first seen (by W. G. C.) June 7, 1944.* He was rejected by the Army on the basis of induction chest roentgenogram. For about six months previously there were times when he was somewhat short of breath, but there were no other symptoms and he had gained twenty pounds during the preceding two years. Past and family history was noncontributory. There was no tuberculosis in the family. Physical examination revealed a well-developed and nourished white man not appearing ill. The lungs were clear to percussion and auscultation. Roentgenograms revealed a sharply circumscribed tumor mass in the posterior mediastinum extending out from the upper pole of the left hilum and measuring about 7 cm. in its greatest diameter. Oral temperature was 99° F., pulse 84, blood pressure 118/80. Laboratory findings were as follows: red blood cells 5.2; hemoglobin 13.5 Gm.; white blood cells 5,850; segmentals 48; lymphocytes 43; mononuclears 8. Sedimentation rate, Westergren method, was 32 mm. in one hour. Urine was negative; blood Wassermann was negative. Sputum negative on concentrate for acid-fast organisms. Bronchoscopic examination elsewhere† was essentially negative except for congestion and edema of the left lower lobe bronchus with some constriction.

The patient was referred to Grasslands Hospital, June 27, 1944, for an exploratory operation. This was done (by G. C. A.) on July 11, 1944, under cyclopropane anesthesia.

From the Division of Diseases of the Chest and the Division of Surgery, Grasslands Hospital, Valhalla, N. Y.

Received for publication June 13, 1949.

*Referred by Dr. R. E. Machan, Mamaroneck, N. Y.

†By Dr. Verne Peterson.

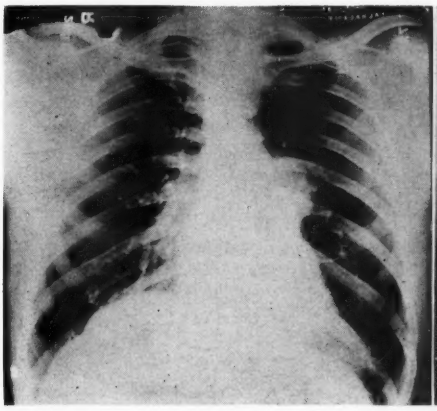


Fig. 1. Fig. 2.

Fig. 1.—Posteroanterior roentgenogram (July 10, 1944) reveals a sharply circumscribed tumor mass in the region of the upper pole of the left hilum measuring approximately 7 cm. in diameter and obstructive emphysema of the left upper lobe.

Fig. 2.—Lateral roentgenogram reveals mass in posterior mediastinum.

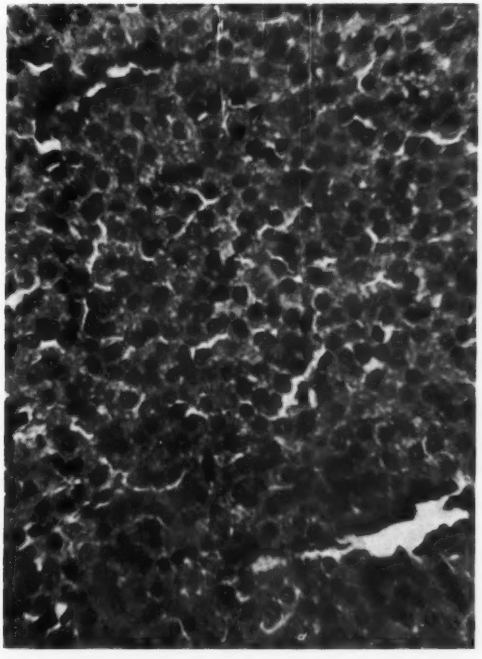


Fig. 3.—High-power field of tumor shows dense array of plasma cells with typical eccentric nuclei. (Magnified.)

A round firm tumor measuring 2 inches in diameter was observed filling the space formed by the arch of the aorta and apparently attached to the pleura superior to the root of the lung. The pleura was incised over the tumor and by careful, sharp dissection the tumor was removed. Postoperative course was uneventful except that the wound healed rather slowly, and the patient remained in the hospital until Aug. 22, 1944, the forty-second postoperative day.

Pathology: The tumor was spindle shaped measuring 6.5 by 3.5 by 3.5 cm. There was a thin capsule enclosing the mass, with several small friable blood-stained nodes present on the surface. Cut section showed the tissue to be rather dark, dry, and friable similar to blood clot. In fact, there was considerable blood throughout, and at times small irregular blood-filled spaces were encountered. In one area, a pattern of thin lines, radiating at right angles from the capsule, was noted. The sections showed a neoplasm composed of masses of mature, but not always typical, plasma cells growing in a very sparse reticular stroma, highly vascularized. The growth was surrounded by a rather thick collagenous capsule which sent heavy trabecular septa into the tumor. Diagnosis* was plasmacytoma.†

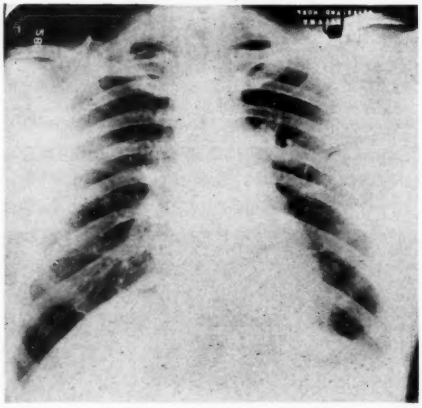


Fig. 4.—Follow-up roentgenogram (Oct. 26, 1948) taken fifty-one months after operation shows no evidence of recurrence.

This patient has been followed by roentgenographic study at intervals since, and except for a virus pulmonary infection in July, 1947, there have been no symptoms referrable to the chest, nearly five years after operation. Roentgenogram on Oct. 26, 1948, revealed no evidence of recurrence.

CASE 2.—H. Y., a 21-year-old white man, was first seen (by W. G. C.) on Jan. 30, 1948.‡ At the time he was employed by a cleaning and dyeing establishment where he claimed to have inhaled formaldehyde fumes. He was separated from the Army in July, 1945, after serving one year, mainly in the Philippines. He had no illness while in the Army, and both induction and separation chest roentgenograms were said to be negative.

He gave a history of a dry hacking cough of about six months duration, and for the previous two months the cough had become productive of about two ounces of yellowish sputum daily. The sputum, on one occasion, was blood-streaked. There were no other symptoms except for a loss of ten pounds during the preceding twelve months. Best weight was 174 pounds, and present weight was 155 pounds. In January he consulted his family physician who obtained chest roentgenograms and a sputum examination, which was found to be negative for acid-fast organisms on direct smear. Subsequent cultures were also negative.

*By Dr. George McClure, Grasslands Hospital pathologist.

†Dr. F. W. Stewart[5] of Memorial Hospital, New York City, studied the sections and concurred in the diagnosis.

‡Referred by Dr. George L. Daniels of Port Chester, N. Y.

Fig. 5.

Fig. 6.

Fig. 5.—Posteroanterior roentgenogram (April 1, 1948) reveals density between the eighth and ninth posterior ribs on the right.

Fig. 6.—Lateral roentgenogram reveals well-circumscribed mass in region of interlobar septum, involving portions of middle and upper lobes.

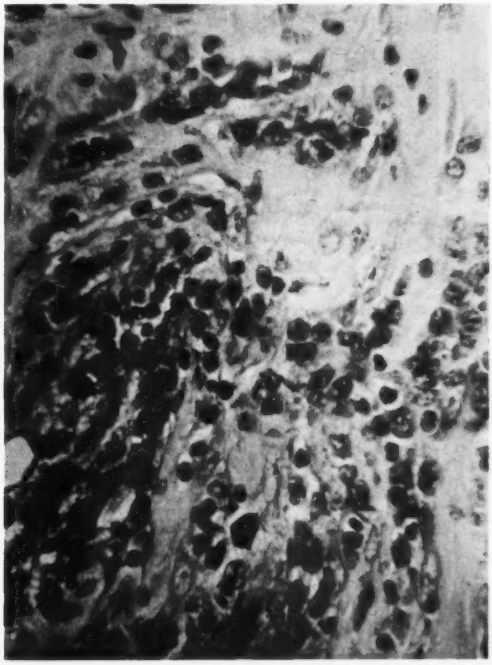


Fig. 7.—High-power field of tumor shows groups of plasma cells in dense fibrous stroma. Lymphocytes and other large mononuclears also present. (Magnified.)

Past and family history was noncontributory. There was no tuberculosis in the family. Physical examination revealed a rather pale but well-nourished white man of about the stated age with entirely normal physical signs. The lungs were clear to percussion and auscultation. The chest roentgenogram revealed a dense, fairly well-circumscribed elliptical mass in the area of the right middle lobe measuring approximately 4 cm. in its greatest diameter. Blood pressure was 108/78. Laboratory findings were as follows: red blood cells 4.95; hemoglobin 14.5 Gm.; white blood cells 7,800; segmentals 74; lymphocytes 22; mononuclears 2; eosinophile 1. Sedimentation rate, Westergren method, was 7 mm. in one hour. Blood chemistry was normal. Bence-Jones protein test was negative; nonprotein nitrogen 35; sugar 80. Blood Wassermann was negative. Sputum and gastric cultures were negative for acid-fast organisms. Other organisms and fungi were not demonstrated. Urine was negative. Bronchoscopic examination* in February, 1948, was reported negative.

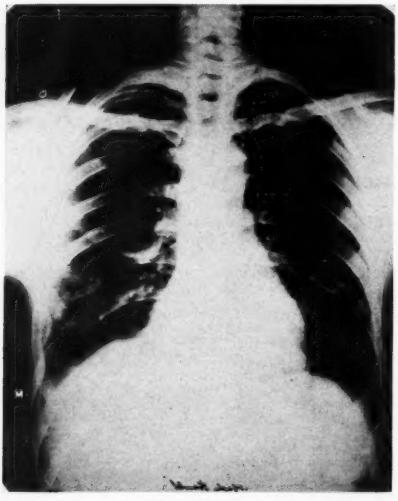


Fig. 8.—Follow-up roentgenogram (Feb. 1, 1949) taken ten months after operation shows no evidence of recurrence.

The patient was admitted to Grasslands Hospital on March 16, 1948, for surgical exploration. It was thought that the lesion seen roentgenographically was probably a benign tumor. Surgical exploration was done (by G. C. A.) on March 23, 1948, and a firm, well-circumscribed mass was found in the right middle lobe, extending through the interlobar fissure and involving a small portion of the right upper lobe. The hilum appeared free of involvement. A frozen section was made and a benign lesion was reported.† Segmental resection was done with removal of most of the right middle and a portion of the right upper lobe. The postoperative course was uneventful and the patient was discharged on April 2, 1948, the twelfth postoperative day. He is back at work, and there are no symptoms.

Pathology: The tumor mass measured 4 by 3 by 3 cm. and was firm. On section the surface was yellow gray in color and streaked with black pigmented strands. It was well demarcated from the surrounding lung tissue, but was not encapsulated. Microscopically the mass was composed of a dense framework of collagenous connective tissue in which was dispersed a variety of cellular forms. Plasma cells were numerous and in areas formed long cords or sheets. Russell fuchsin bodies, intracellular and extracellular, were frequently en-

*By Dr. M. T. Smith of New Rochelle, N. Y.
†By Dr. S. Gross, acting pathologist at Grasslands Hospital.

countered. Lymphocytic aggregates were abundantly present, as were many incorporate reticulum cells. No Reed-Sternberg giant cells were seen. Eosinophiles were generously scattered throughout. Remaining alveoli present in the mass were often filled with large foamy macrophages. Microscopically the mass was not so well circumscribed as described grossly. The interlobar fissure and pleura were markedly thickened.*

Plasma cells have been considered to be differentiated lymphocytes, normal constituents of connective tissue originating from tissue lymphocytes, or emigrated blood lymphocytes. Functionally they have been thought to be related to immunization processes, of elaborating antitoxic substances, and capable of removing cellular metabolic products. Plasma cell tumors occur frequently in the bone marrow, but extramedullary plasma cell tumors are more rare and originate more often in the upper respiratory tract. They may be single or multiple, noncancerous or cancerous, with or without metastases. They more frequently metastasize to bones and lymph nodes. Eggston[6] has observed that plasmacytomas in the upper respiratory tract become malignant in some instances. He states that an increase in plasma cells may occur in a variety of chronic inflammatory conditions such as tuberculosis and syphilis, to such a degree as to simulate true neoplasm.

In both of our cases symptoms had existed for approximately six months and in Case 1 were undoubtedly due to pressure. However, in Case 2 there were productive cough, blood-streaked sputum, and loss of weight, symptoms not uncommon in pulmonary infection. There has been no evidence of recurrence in Case 1 in more than four years observation, or in Case 2 in ten months observation.

REFERENCES

1. Hellwig, C. A.: Arch. Path. **36**: 95, 1943.
2. Gordon, Joseph, and Walker, Gerald: Arch. Path. **37**: 222-224, 1944.
3. Bross, K.: Folia haemat. **45**: 137, 1931, cited by Hellwig.[1]
4. Klose, H.: Beitr. z. klin. Chir. **74**: 20, 1911.
5. Stewart, F. W.: Personal communication.
6. Eggston, A. A., and Wolff, D.: Histopathology of the Ear, Nose and Throat, Baltimore, 1947. Williams & Wilkins Company.

*Dr. Gross, suspecting a plasma cell tumor, consulted Dr. F. W. Stewart, of Memorial Hospital, New York City, who attached the diagnosis of "plasma cell granuloma of lung." He stated that he had seen two or three similar examples and believed that they are not tumors, but represent inflammatory granulomatous lesions of unknown etiology.

LEIOMYOMA OF THE ESOPHAGUS

ROLLIN A. DANIEL, JR., M.D., AND R. B. WILLIAMS, JR., M.D.
NASHVILLE, TENN.

BENIGN neoplasms of the esophagus are observed very infrequently. The leiomyoma is probably the most common benign tumor which arises in the esophagus. Patterson[1] reviewed the literature between the years 1717 and 1930 and found only 62 benign tumors reported, all of which were found at autopsy. The type of each tumor was not listed. Rose[2] reported 49 cases of leiomyoma of the esophagus found in the literature between 1797 and 1932 and added 1 of his own. All were found at autopsy. Moersch and Harrington[3] report 44 cases of benign tumor of the esophagus found in 7,459 necropsies at Mayo Clinic. Thirty-two of these are leiomyomas. In 4,000 autopsies at the Vanderbilt University Hospital no case of leiomyoma of the esophagus was found.

It is evident that most leiomyomas of the esophagus do not produce symptoms. Moersch and Harrington[3] report that in 11,000 patients complaining of dysphagia studied at Mayo Clinic only 15 benign tumors of the esophagus were found. Of these 2 were definite leiomyomas. In 3 others the diagnosis was listed as undetermined but probably leiomyoma. In none of the 32 leiomyomas found at autopsy at the Mayo Clinic were symptoms produced by the tumors.

Few cases of myoma of the esophagus have been discovered in the living patient. A search of the literature reveals that only 8 patients have been operated upon for removal of such a tumor. In 2 of these the tumor involved the cardia of the stomach as well as the esophagus, so their primary site could not be definitely determined.

Ohsawa[4] reported a 43-year-old woman who complained of dysphagia of twenty-four hours duration and was found to have esophageal dilatation. In performing an esophagocardioplasty for relief of cardiospasm, an unsuspected submucosal myoma 1 cm. in diameter was found and enucleated. The patient survived the procedure.

Brock[5] reported a male patient, aged 47 years, with leiomyoma of the esophagus, who complained of weakness, vomiting, pain in the right hypochondrium, loss of appetite, indigestion, and dragging sensation in the left side. At operation a lobulated mass measuring 10 by 7 cm. was found high on the lesser curvature of the stomach extending above and below the diaphragm. The distal end of the esophagus and the cardia of the stomach including the tumor was removed and an esophagogastrostomy performed. The patient recovered. This tumor involved the wall of both the esophagus and the stomach.

Harrington and Moersch[6] reported a male patient, aged 38 years, with a leiomyoma of the esophagus who complained of nervousness and fatigue of four months' duration but no dysphagia. There was marked deformity of the lower

From the Department of Surgery, Vanderbilt University School of Medicine.
Received for publication June 13, 1949.

third of the esophagus with angulation to the left. At operation a tumor was found to involve the entire wall of the lower third of the esophagus, down to the cardia of the stomach. The lower esophagus and the cardia of the stomach were resected. The patient died on the fourth postoperative day of bilateral bronchopneumonia.

The same authors reported another patient, a woman, aged 56 years, who complained of pain beneath the xiphoid but no dysphagia. A large leiomyoma was found to involve the lower part of the esophagus with the greater part of the tumor in the posterior mediastinum and extending through the esophageal hiatus into the abdomen. The mucous membrane was intact. The tumor was excised locally except for a small portion attached to the pericardium which was left. Her postoperative course was uneventful. This tumor may have arisen from the stomach.

Harper and Tiscenco[7] reported a male patient, aged 41 years, with a leiomyoma of the esophagus who for three years had had a feeling of tightness in the epigastrium following meals, which was relieved by vomiting. A submucosal tumor 6 by 3 cm. in size was found in the right posterior lateral wall of the middle third of the esophagus. The mucous membrane was intact and the pedicle was composed of avascular fibrous tissue. The tumor, a leiomyoma, was removed. The patient died on the fourth postoperative day and at post-mortem examination "wet lungs" were found.

Calmenson and Clagett[8] reported a male patient, aged 52 years, who complained of substernal distress associated with slight difficulty in swallowing which occurred twice a year for ten years. Two leiomyomas were found in the wall of the esophagus at operation. They were located near the arch of the aorta and measured 2 and 6 cm. in diameter. Both tumors were removed without opening the esophageal mucosa. The patient's postoperative course was uneventful.

Schafer and Kittle[9] reported a male patient, aged 46 years, who complained of epigastric distress and bilateral costovertebral angle pain with associated nausea and vomiting. There was no dysphagia. Roentgen examination of his thorax revealed a large rounded area of increased density in the lower posterior mediastinum displacing the esophagus to the right. At operation a lobulated, sharply delineated mass 7 by 7 by 10 cm. in size was found 6 cm. above the diaphragm. Removal of the tumor required excision of an ovoid section of the wall of the esophagus. The postoperative course was uneventful. Microscopically the tumor was a leiomyoma.

Hurwitz[10] reported a male patient, aged 31 years, who entered the hospital for repair of an inguinal hernia. Routine roentgenogram of the chest revealed an ovoid shadow, 3 by 5 cm. in size just to the right of the midline and superimposed on the right heart border. Exploration of the chest was performed and a leiomyoma was found, one inch below the azygos vein protruding through the longitudinal muscle fiber of the esophagus and encircling three-quarters of it like a collar. The tumor was removed without opening the mucosa. The postoperative course was uneventful.

CASE REPORT

A 38-year-old, white, married, female schoolteacher was admitted to the Vanderbilt University Hospital in December, 1947. She was told following routine chest examination six months previously that she had a growth in the right chest. She had had no cough, dysphagia, dyspnea, chest pain, nausea, vomiting, or any other symptoms referable to the chest. Physical examination revealed a well-developed and well-nourished woman. There were no abnormal physical findings. On chest roentgenogram (Fig. 1) a well-demarcated, homogeneous area of increased density measuring 6.5 by 6 cm. was seen in the right hemithorax overlying the medial aspect of the dome of the right diaphragm. Roentgen examination of the esophagus with barium showed some displacement of the esophagus to the left by the mass but no obstruction. There was a small paraesophageal hiatal hernia.

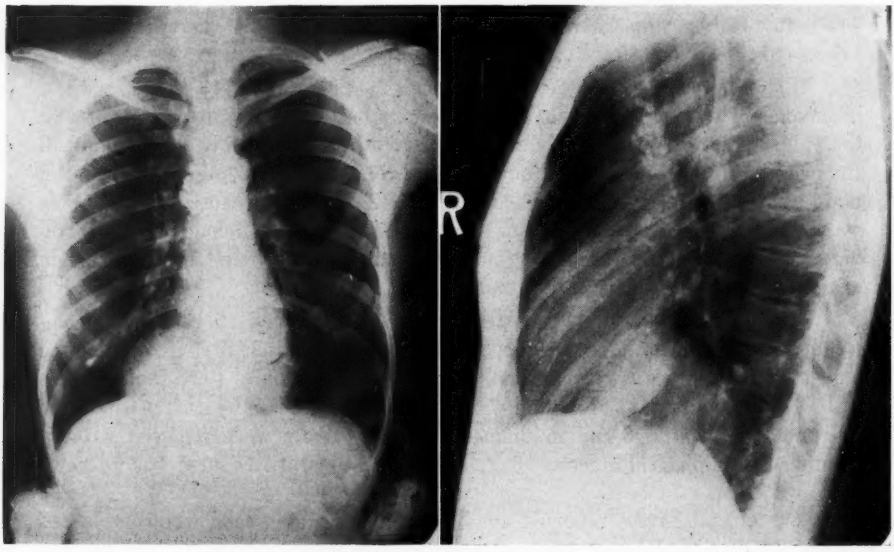


Fig. 1.—Roentgenograms made Dec. 29, 1947, one day prior to operation.

At operation on Dec. 30, 1947, a posterolateral incision was made over the ninth rib. A long segment of the ninth rib was removed subperiostally and the pleura opened. The lower lobe of the right lung was retracted upward and a firm, encapsulated, nodular mass about 7 cm. in diameter was present beneath the mediastinal pleura and posterior to the inferior pulmonary ligament. The mediastinal pleura was opened over the mass and the mass separated from the surrounding loose connective tissue. It was delivered into the pleural cavity and found to be attached to the esophagus by a pedicle 3 cm. long. It was easily freed from the wall of the esophagus by dividing the esophageal muscle and exposing the mucous membrane. The esophageal mucosa was not opened. Following removal of the tumor, the edges of the esophageal muscle were brought together with interruptéd fine silk sutures. The lung was inflated and the wound of the chest wall closed in layers with interrupted fine silk sutures. The patient stood the procedure very will.

The postoperative course was uneventful. Wangensteen suction was instituted but discontinued on the second postoperative day and the patient started on a liquid diet. On the fifth day the patient was started on a soft diet which she took well. On the seventh postoperative day roentgen examination of the esophagus with barium revealed some in-

constant irritability in the esophagus about three inches above the diaphragm. The mucosal pattern appeared normal and there was no delay in passage of barium. Chest roentgenogram made on the eighth postoperative day showed a small mount of fluid at the base of the right lung and a slight residual collapse of the lower and middle lobes of the right lung.

The patient was discharged on the ninth postoperative day. Chest roentgenogram (Fig. 2) made about seven weeks following the operation revealed no abnormality other than a small amount of fluid at the base of the right lung and incomplete expansion of the lower and middle lobes of the right lung. She was and has remained asymptomatic.

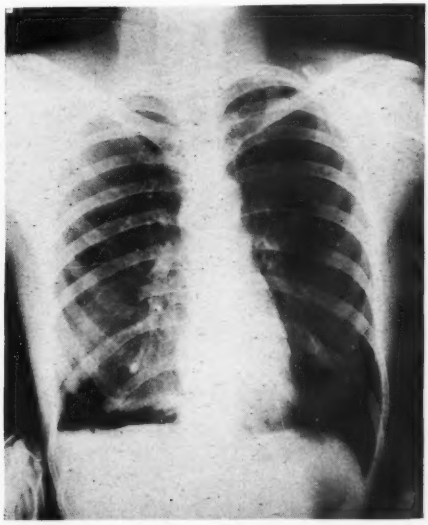


Fig. 2.—Roentgenogram made Feb. 16, 1948, seven weeks following operation.

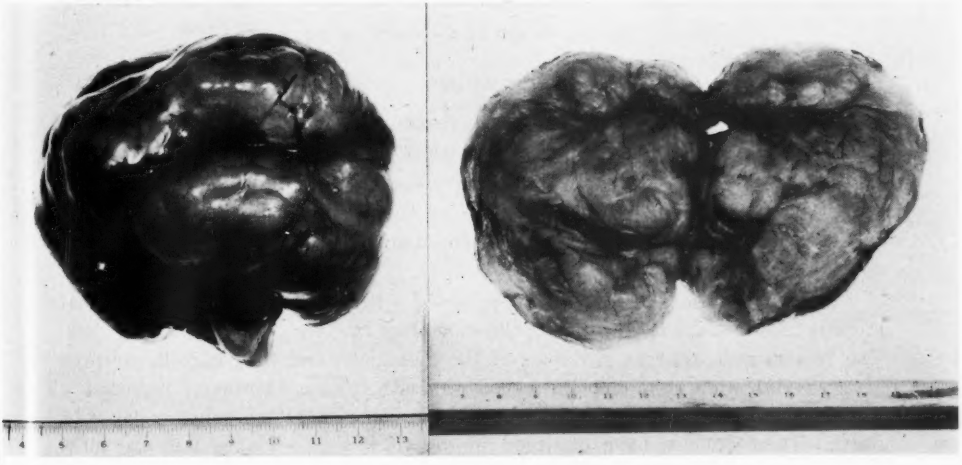


Fig. 3.—Photograph of the tumor following its removal.

Examination of the gross specimen (Fig. 3) revealed a smooth, well-encapsulated, firm tumor with a lobulated surface and a pale, yellowish white color. The capsule was unbroken. On cut surface the tumor was yellowish in color and homogenous in appearance with grossly visible whorls. Some areas were firmer than others. No cysts were present.

Microscopic section (Fig. 4) of the tumor revealed strands of smooth muscle with long spindle-shaped cells with eosinophilic cytoplasm. The nuclei were short, stubby and uniform. No mitotic figures were present. This muscle was arranged in whorls. Masson stain revealed that connective tissue comprised grossly one-third of the total tissue.

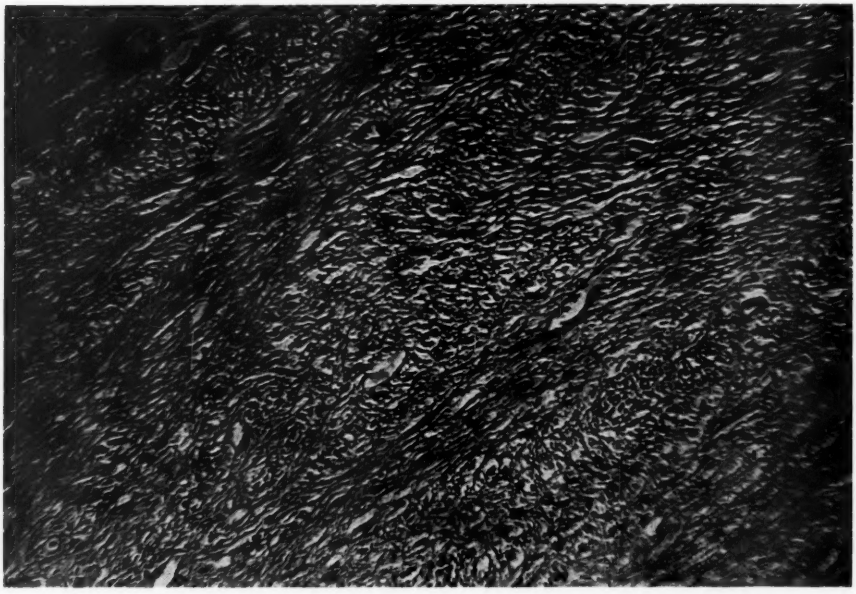


Fig. 4.—Photomicrograph of the tumor (about ×400).

COMMENT

Ninety-two cases of leiomyoma of the esophagus have been reported in the literature.[2-12] One was complicated by islets of adenocarcinoma. Of the 92 patients, 8 were operated upon and 6 survived. In 2 of the 8, the tumor involved the cardia of the stomach as well as the esophagus so the primary site is not certain. Of the 6 patients in whom the diagnosis is certain, 4 survived operation.

Many of these tumors can be removed without opening the esophageal mucous membrane. In such cases the mortality rate should be extremely low. The tumors may arise at any level of the esophagus and they may be solitary or multiple but seldom are the cause of death. Rose,[2] however, reported a patient, aged 74 years, in whom multiple leiomyomas were the primary cause of death. These tumors have occurred in individuals of all ages but are most common in elderly people. They are more frequent in men.

REFERENCES

1. Patterson, Ellen J.: Benign Neoplasms of the Esophagus, Pennsylvania M. J. **36**: 244-246, 1933.
2. Rose, J. Dudfield: Myomata of Esophagus, Brit. J. Surg. **24**: 297-308, 1936.
3. Moersch, Herman J., and Harrington, Stuart W.: Benign Tumor of the Esophagus, Ann. Otol., Rhin. & Laryng. **53**: 800-817, 1944.
4. Ohsawa, T.: The Surgery of the Esophagus, Arch. f. jap. Chir. **10**: 605-700, 1933.
5. Brock, R. C.: Cardio-Esophageal Resection for Tumor of the Cardia, Brit. J. Surg. **30**: 146-150, 1942.
6. Harrington, S. W., and Moersch, H. J.: Surgical Treatment and Clinical Manifestations of Benign Tumors of the Esophagus With Report of Seven Cases, J. THORACIC SURG. **13**: 394-414, 1944.
7. Harper, R. A. Kemp, and Tiscenco, Eugene: Benign Tumor of Esophagus and Differential Diagnosis, Brit. J. Radiol. **18**: 99-107, 1945.
8. Calmenson, Marvin, and Clagett, O. Theron: Surgical Removal of Leiomyomas of the Esophagus, Am. J. Surg. **72**: 745-747, 1946.
9. Schafer, Paul W., and Kittle, C. Frederick: Esophageal Leiomyoma, J. A. M. A. **133**: 1202-1205, 1947.
10. Hurwitz, Alfred: Leiomyoma of the Esophagus, Surgery **25**: 304-306, 1949.
11. Ewing, James: Neoplastic Diseases, ed. 4, Philadelphia, 1940, W. B. Saunders Co., p. 237.
12. Barazzuol, E.: Contributo alla Studio dei Tumori Muscolari dell'esofago, Arch. ital. d. mal. d. app. diger. **9**: 41-50, 1940.

LEIOMYOMA OF THE LUNG

R. B. Williams, Jr., M.D., and Rollin A. Daniel, Jr., M.D.
Nashville, Tenn.

PRIMARY leiomyoma of the lung is rare. Review of the literature reveals that only four have been reported. Brahdy[1] reported a case in a young woman, aged 18 years, who was being studied as a tuberculous suspect. Roentgenogram of the chest showed a 1.6 cm., round area of density at the right lung base. X-ray examination of the chest made six months previously had shown no abnormality. The sputum became positive for acid-fast bacilli and in nineteen months a typical tuberculous infiltration was found in the right upper lung field. The mass at the right base gradually increased until three years later its diameter was approximately twice the original. Surgical exploration of the chest was done at this time and a "localized," round mass 2.5 cm. in diameter was found in the lower lobe of the right lung. The lower two-thirds of the lobe including the tumor was removed. The patient made an uneventful recovery. On cut surface the tumor was firm and white. Microscopic section revealed it to be a fibroleiomyoma.

Forkel[2] reported a case of leiomyoma of the lung found at autopsy on a woman, aged 63 years, who died of pneumonia. The "lemon-sized" mass was found in the apex of the upper lobe between the second and fourth ribs. Deussing[3] reported a woman, aged 57 years, with multiple primary myomas of the lung found at autopsy. Franco[4] reported an autopsy on a 56-year-old woman in whom a 13 by 11 by 9 cm. mass was found in the upper lobe of the left lung. This tumor was thought to be a leiomyoma.

CASE REPORT

On Jan. 18, 1947, an 8-year-old white girl was seen in the Vanderbilt University Hospital Pediatric Clinic complaining of a chronic cough of four years' duration. The cough was productive of clear mucoid sputum. There had been no pain, dyspnea, orthopnea, hemoptysis, weight loss, cyanosis, or retardation of growth. The child had done well in school and carried on normal physical activity without noticeable difficulty. Physical examination revealed some cervical lymph node enlargement and mild rhinitis. Physical examination of the thorax and lungs revealed no abnormal findings. Chest roentgenogram (Fig. 1) was made and interpreted as showing no abnormality. Allergy skin tests were made and several positive reactions obtained. Desensitization consisting of weekly injections of allergen was begun.

The cough after ten months was not improved. She was found at this time to have absence of breath sounds over the lower left thorax posteriorly. Roentgenogram of the chest was repeated and revealed a dense opacity measuring 10 by 7 cm. lying posteriorly over the mid-portion of the left diaphragm (Fig. 2). The original x-ray film of the chest was reviewed and the mass could be seen in the same location but was smaller and partially obscured by the heart shadow.

From the Department of Surgery, Vanderbilt University School of Medicine.
Received for publication June 13, 1949.

The patient was admitted to Vanderbilt University Hospital and roentgen examination of the esophagus and stomach with barium was done. No filling defect or dilatation was present in either the esophagus or cardia of the stomach. Bronchoscopy revealed narrowing of the left bronchus as it passed into the lower lobe, but no ulceration or other abnormalities were seen.

On Nov. 15, 1947, under nitrous oxide, oxygen and ether inhalation anesthesia, exploration of the chest was made. A posterolateral incision was made over the left sixth rib and a long segment of this rib removed subperiosteally. The incision was extended through

Fig. 1.—Roentgenogram made Feb. 15, 1947, nine months prior to operation.

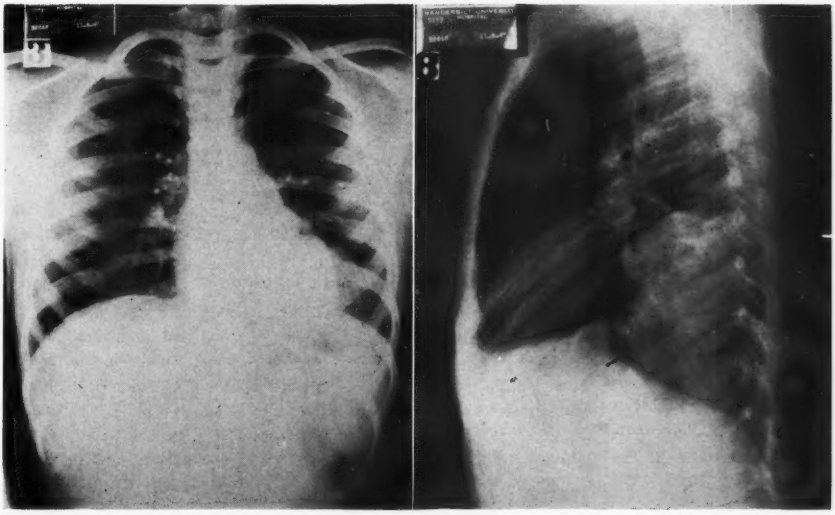


Fig. 2.—Roentgenograms made Nov. 8, 1947, one week prior to operation.

the periosteum and parietal pleura opening the hemithorax. A very large and extremely hard nodular tumor was found in the lower lobe of the left lung. This mass occupied at least one-half of the lower lobe, extending from the hilum laterally to the visceral pleura and downward to the diaphragm. The left lower lobe was densely adherent to the diaphragm over an area about 3 cm. in diameter and there were a large number of short dense adhesions between the lower lobe and the posterior chest wall. These adhesions were freed by sharp dissection and the lobe was freed from the diaphragm in the same manner. The fissure between the upper and lower lobes was quite distinct. The tumor was found to envelope the lower lobe bronchus and was firmly and densely adherent to it. What was thought to be the lower lobe bronchus was freed and occluded, but on inflating the lung this was found to be the upper lobe bronchus and it became evident that the lower lobe bronchus could not be exposed. Because of this and because the gross appearance of the tumor suggested that it might be malignant, pneumonectomy was performed. Following irrigation of the pleural cavity with saline, the wound of the chest wall was closed in layers with interrupted fine silk sutures.

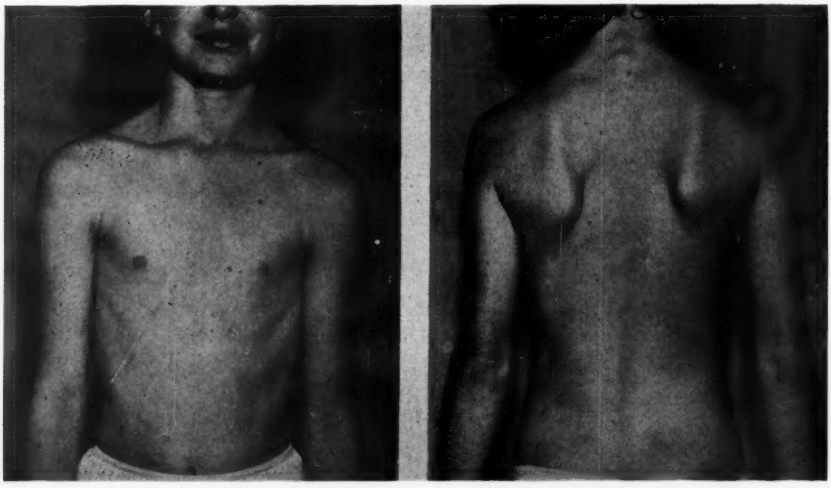


Fig. 3.—Photograph made April 16, 1949, seventeen months following pneumonectomy.

The postoperative course was uncomplicated. She reacted well and only on one occasion had rectal temperature over 100.4° F. On the second postoperative day thoracentesis was performed and 120 c.c. of bloody fluid and 80 c.c. of air were removed. She was afebrile after the third postoperative day. She received parenteral penicillin for six days postoperatively and was discharged from the hospital seven days after operation.

Since discharge the patient has had no serious difficulty. She has had occasional upper respiratory infections and her activities at school and at home have not been restricted. She has very little deformity of her thorax (Fig. 3). Roentgenogram of the chest made on Jan. 27, 1949, revealed the right lung to be clear. The lower one-half of the left hemithorax was opaque. The trachea and the heart were displaced markedly to the left.

Examination of the specimen (Fig. 4) after operation revealed the left lung to weigh 252 Gm. In the lower lobe was an oval, slightly nodular, firm, rubbery, pale white tumor measuring 7 cm. in diameter, presenting at the posterior, lateral, and inferior surfaces of the lung. The pleura covering the tumor was smooth and glistening. The lower lobe

bronchus for almost its entire length was surrounded by the tumor and was obliterated by it. The cut surface of the tumor was pale yellow at the periphery with a central core which was light yellow and opaque with some diffuse calcification.

Microscopic sections (Fig. 5) showed the tumor to be composed of large whorls of spindle-shaped cells with elongated nuclei separated by collagenous connective tissue septa.

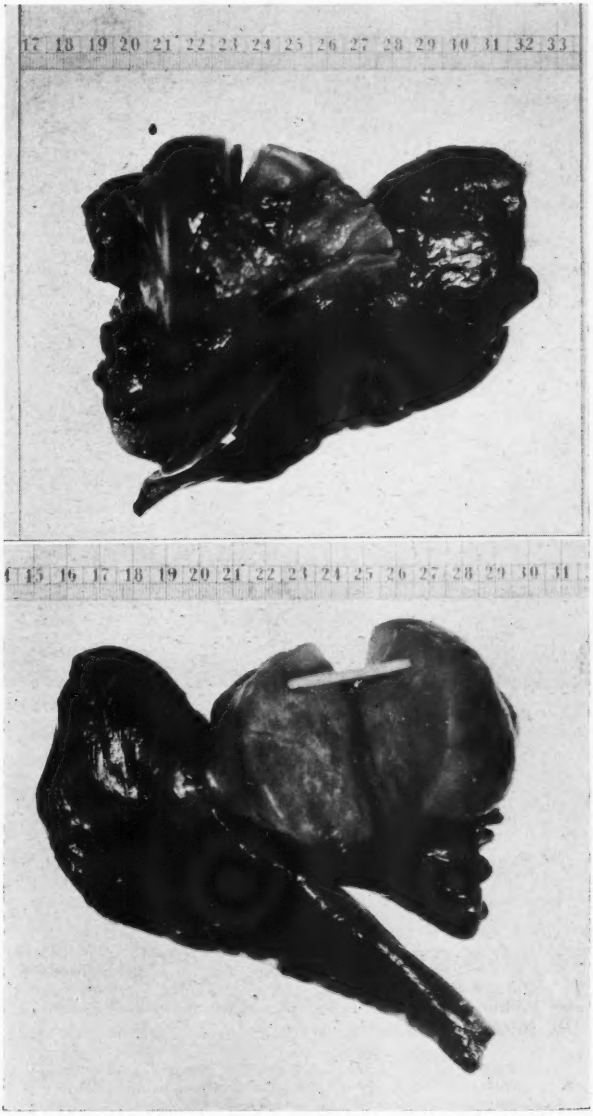


Fig. 4.—Left lung with leiomyoma in the lower lobe.

Some pallisading of cells and calcification was present. Where the spindle-shaped cells were cut at right angles, they, as well as their nuclei, appeared round. A large number of spaces lined with a single layer of endothelium and containing red blood cells were present throughout the tumor. With Masson's stain the whorls of spindle-shaped cells were brick red in color while the fibrous tissue septa were green. The tumor was surrounded by a thin fibrous tissue capsule.

The final diagnosis was leiomyoma of the lung.

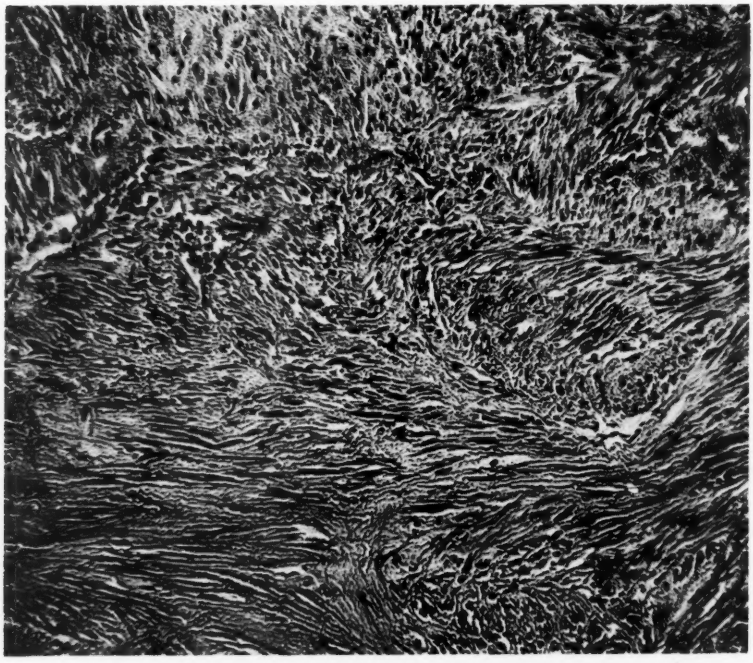


Fig. 5.—Photomicrograph of the tumor (about ×400).

SUMMARY

A report of a patient with a leiomyoma of the lung treated by pneumonectomy is given. Four similar patients have been reported. One of these was successfully operated upon and in the other three, the tumors were found at autopsy.

REFERENCES

1. Brahdy, Leopold: Leiomyoma of Lung, Am. Rev. Tuberc. **43**: 429-434, 1941.
2. Forkel, W.: Ein Fall von Fibromyom der Lunge, Ztschr. f. Krebsforsch. **8**: 390-393, 1910.
3. Deussing, R.: Multiple Primary Myomas of Lung, Thesis, University of Munich, 1912.
4. Franco, Enrico Emilio: Sopra un rarissimo voluminoso leiomioma del polmone, Tumori **15**: 27-42, 1929.

AN APPARENTLY CONGENITAL BRONCHOESOPHAGEAL FISTULA PERSISTENT TO ADULT LIFE

DOUGLAS R. MORTON, M.D., JOHNSTON F. OSBORNE, M.D., AND
KARL P. KLASSEN, M.D.
COLUMBUS, OHIO

DURING the past decade significant progress in the field of thoracic surgery, together with the addition of chemotherapy and antibiotics to our therapeutic armamentarium, has accomplished the successful management of many cases of abnormal esophageal communications. These esophageal fistulas are classified into two main types: congenital and acquired. The latter is encountered most frequently, and may exist for a length of time without producing symptoms; in some instances it is even compatible with a relatively comfortable existence for a number of months. The congenital type invariably manifests itself with the first effort at swallowing, and if not recognized it is supposed uniformly to result in early death of the infant.

Monserrat[1] reported a series of 670 cases of esophageal fistula which illustrated the preponderance of the acquired type. Three hundred sixty-seven were associated with neoplasm, 222 were congenital, 41 were due to infection, and 40 were traumatic in their origin. Moersch and Tinney[2] in 1944, and Abbott[3] in 1945, added additional cases; however, these reports were limited to the acquired type and revealed etiological factors similar to those of Monserrat. The most common causes of the acquired type of esophageal fistulas are esophageal and bronchial carcinoma, neoplasm of neighboring structures, for example, Hodgkin's disease, tuberculosis (empyema and periadenitis), syphilis, and trauma. Rarer cases have been reported secondary to esophageal stricture, diverticulum, esophagitis, actinomycosis, syphilitic aneurysm, vomiting, alcoholism, and cardiospasm.

Vogt[4] classified congenital esophageal anomalies into three main types as follows:

Type I. Complete absence of the esophagus.
Type II. Atresia of the esophagus with an upper and lower esophageal segment, each ending in a blind pouch.
Type III. Atresia of the esophagus with tracheoesophageal fistula.
(a) With fistula between upper segment and trachea.
(b) With fistula between lower segment and trachea.
(c) With fistula between both segments and trachea.

The congenital anomalies have been presented by Haight and Towsley,[5] Ladd,[6] and Holt, Haight, and Hodge.[7] The latter group found 91.3 per cent of

From the Department of Research Surgery, The Ohio State University.
Aided by a Grant from the Mary Christie Curtis Fund for Surgical Research of The Ohio State University.
Received for publication June 24, 1949.

a series of 46 cases to be of Type III (b). However, one of their cases presented particular diagnostic difficulty, for which they suggested the addition of another type to Vogt's classification: single tracheoesophageal fistula without atresia.

Because of the rarity of this condition, the following case of an apparent congenital bronchoesophageal fistula persistent to adult life and associated with unilobar bronchiectasis is presented.

CASE REPORT

J. G. S. (No. 484971), a 26-year-old white male university student was admitted to University Hospital June 16, 1948, complaining of cough of several years' duration. Following pertussis at the age of 4 years, he had noted a mild, persistent cough. Although he was seriously ill with pneumonia at 5 years of age, there was no definite increase in his cough. Other than his main complaint he remained in relatively good health until shortly after his entrance into the Army in 1942. After eight months' hospitalization for continuous colds, productive cough (1 cup per day), fever, chills, and weight loss of fifty pounds, he received a medical discharge from the Army, the diagnosis being bronchiectasis. Although there was some subsidence of complaints following discharge from the Army, he noted seasonal exacerbation of symptoms.

Fig. 1.—Admission bronchogram which reveals severe saccular bronchiectasis of the posterior basal segment of the right lower lobe. Arrow points to bronchoesophageal fistula.

On physical examination the essential findings were limited to the chest, there being slight dullness and decreased breath sounds in the right posterior base. All laboratory data were within normal limits. Chest roentgenograms revealed an increased density in the region of the right posterior basal segment. There was a shift of the heart to the right with slight elevation of the diaphragm. A bronchogram showed severe saccular bronchiectasis of the posterior basal segment of the right lower lobe. The changes in the anterior basal segment were less severe (Fig. 1).

The patient was placed on systemic and aerosol penicillin two days preoperatively, resulting in a definite decrease in sputum production.

On the fifth hospital day under general endotracheal anesthesia a right posterolateral thoracotomy incision was made. After subperiosteal transection of the sixth and seventh ribs at their posterior angles, the chest was entered through the sixth intercostal space. On exploration there was moderate fibrosis and evidence of bronchiectasis in the posterior portion of the right lower lobe. Fine adhesions between the parietal and visceral pleura were divided. The pulmonary ligament was divided and the inferior pulmonary vein was ligated. During this process there was discovered a tubal structure about 5 cm. long and 5 mm. in diameter, which extended from the right anterolateral aspect of the esophagus at about the level of the ninth thoracic vertebra to the substance of the hilus of the right lower lobe posteriorly, about 1 cm. below the bifurcation of the right middle and lower lobe bronchi (Fig. 2). The tubal structure was isolated easily, doubly ligated with fine silk, and upon sectioning exhibited the characteristics of the gastrointestinal tract. The proximal stump was further closed with two over-end fine silk sutures at its origin in the esophagus. The right lower lobe was then removed, using the individual ligation technique. After instillation

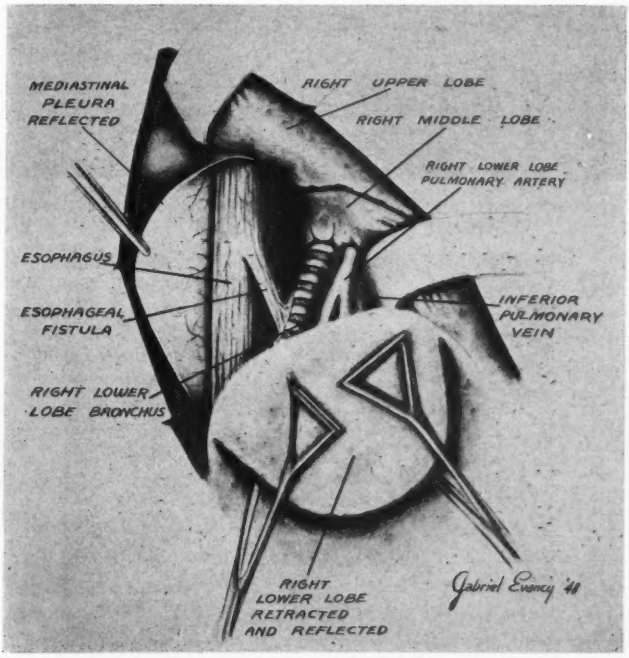


Fig. 2.—Diagrammatic illustration of relationship of structures as seen at surgery.

of 100,000 units of penicillin, the thorax was closed in a routine manner with a Pezzar catheter placed through a stab wound in the anterior axillary line. The drainage catheter was connected to a water-trap drainage bottle and removed forty-eight hours postoperatively, at which time the right lung was well expanded.

Study of the surgical specimen revealed a right lower lobe weighing 240 Gm. and measuring 10 by 10 by 8 cm. On its mediastinal surface there was a fistulous tract 2 cm.

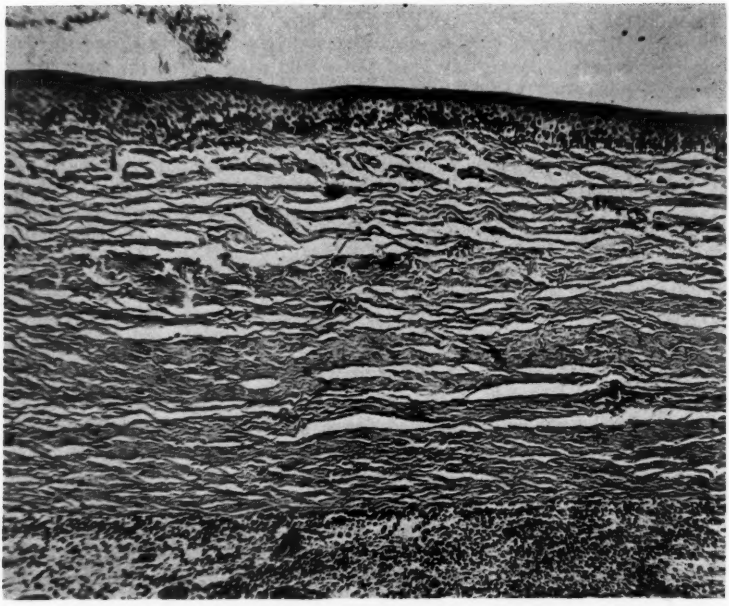


Fig. 3.—Microphotograph (×10) of bronchoesophageal fistula. Note squamous-cell epithelium.

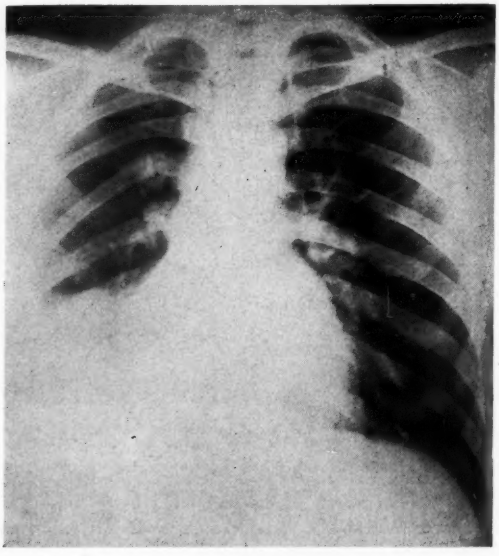


Fig. 4.—Roentgenogram of chest six weeks following right lower lobectomy.

in length and 5 mm. in diameter arising from the right lower lobe bronchus. The fistula was opened and was seen to contain a collection of mucus and an undigested pickle rind. The remainder of the lung was atelectatic with dilatation of the main bronchi. Microscopic sections revealed the fistulous tract to be composed of smooth muscle tissue and lined with thin stratified squamous epithelium (Fig. 3). The remainder of the lobe revealed the microscopic appearance of advanced bronchiectasis.

A review of the history was undertaken with specific questioning of the patient and his relatives. The mother had hyperemesis gravidarum during carriage of the patient. There was no difficulty in nursing or swallowing as an infant. The patient volunteered the following symptomatology which was previously withheld because other physicians had labeled him as a psychoneurotic.

During his eight months' hospitalization in an Army hospital he complained of continuous upper respiratory infection, congested nose, general malaise, myalgia, and chills and fever. It was at this time that the cough and sputum production were definitely increased, and it was noted that the paroxysms of coughing and choking sensations were initiated by ingesting fluids. "It seemed as if something was dripping into the lungs which had to be coughed up." On many occasions he coughed up coffee grounds, pea hulls, and bread crumbs. There was no associated vomiting or regurgitation. These paroxysms were more frequent when lying down, especially when on the left side.

The patient was discharged greatly improved on the thirteenth hospital day. Six weeks postoperatively he was asymptomatic and a roentgenogram revealed minimal postoperative pleural thickening (Fig. 4). During the year since surgery the symptoms have completely subsided; he has gained weight, and is doing well in his schoolwork.

DISCUSSION

The preceding case presents two pathologic entities, a congenital bronchoesophageal fistula and right lower lobe bronchiectasis. We assume the fistula to be congenital inasmuch as the tract was such a well-defined tubal structure that when first seen in the hilar substance it was mistaken for an accessory blood vessel. However, transection of the tube exhibited the characteristics of the gastrointestinal tract and was followed proximally to its entrance into the esophagus. The adhesions encountered at surgery, although prominent over the bronchiectatic lobe, were absent over the proximal one-half of the fistulous tube.

Although cough had been present since infancy, the typical symptoms of congenital esophageal fistula did not become manifest until the patient had reached adult years. Unfortunately these typical symptoms were loosely labeled "psychoneurotic," and the patient hesitated before volunteering the information which aided in making a correct diagnosis of the condition as found at surgery.

SUMMARY

1. A case of congenital bronchoesophageal fistula with secondary bronchiectasis in an adult is presented.

2. The onset of the typical symptomatology of a congenital bronchoesophageal fistula did not become manifest until adult life. Right lower lobectomy and closure of the esophageal fistula resulted in complete recovery.

REFERENCES

1. Monserrat, J. L.: Fistulas tuberculosas esofago-traqueo-bien quicas, Rev. Asoc. med. argent. **55:** 438, 1941.
2. Moersch, H. J., and Tinney, W. S.: Fistula Between the Esophagus and the Tracheobronchial Tree, M. Clin. North America **28:** 1001, 1944.
3. Abbott, O. A.: Abnormal Esophageal Communications: Their Types, Diagnosis and Therapy, J. THORACIC SURG. **14:** 382-392, 1945.
4. Vogt, E. C.: Congenital Esophageal Atresia, Am. J. Roentgenol. **22:** 463, 1929.
5. Haight, C., and Towsley, H. A.: Congenital Atresia of the Esophagus With Tracheo-Esophageal Fistula, Surg., Gynec. & Obst. **76:** 672-688, 1942.
6. Ladd, W. E.: The Surgical Treatment of Esophageal Atresia and Tracheo-Esophageal Fistula, New England J. Med. **230:** 625-637, 1944.
7. Holt, J. F., Haight, C., and Hodges, F. J.: Congenital Atresia of the Esophagus and Tracheo-Esophageal Fistula, Radiology **47:** 457-470, 1946.

A NEW METHOD OF AUTOMATIC CONTROLLED RESPIRATION

MILTON H. ADELMAN, M.D., ROBERT A. BERMAN, M.D.,* AND
ARTHUR S. W. TOUROFF, M.D.
NEW YORK, N. Y.

CONTROLLED respiration may be defined as an anesthetic technique in which apnea is intentionally induced and respiration then maintained by intermittent inflation of the lungs. First described by Guedel and Treweek[1] in 1934, it now is considered by many surgeons and anesthesiologists to be a valuable aid in thoracic surgery.[2-5] The development of mechanical devices to maintain controlled respiration automatically was inevitable and the Scandinavian workers have been pre-eminent in the field. Thus, in 1940, Crafoord[5] of Stockholm described the Crafoord-Frenckner spiropulsator and its successful application to thoracic surgery. Moerch[7] of Denmark, in 1947, reported a respirator of original design for automatic control of respiration. Mautz,[6] one of the pioneers in our own country, presented his experiences with a mechanical respirator for automatic and augmented breathing in 1941.

In our approach to the problem of automatic controlled respiration, we held the belief that there was need for an apparatus less complicated than those described by the aforementioned workers. Thus, when Harroun and co-workers[8] reported their pentothal-curare apneic technique in transthoracic surgery, it occurred to us that some simple automatic device could be adapted to the Harroun technique in order to maintain controlled respiration more effectively than by manual methods. The pneumatic balance resuscitator appeared to be such a device.

The pneumatic balance resuscitator (PBR)† is a light, simple, sturdy apparatus which permits of effective cleansing and sterilization. It was developed by Burns[9] and studied extensively by Motley and co-workers.[10] In brief, the PBR consists of a differential pressure valve which converts continuous positive pressure into intermittent positive pressure. Changes in positive pressure are obtained through a pressure-regulating device attached to the source of continuous pressure (oxygen cylinder). The differential pressure valve requires no adjustment. A nebulizer can be incorporated into the PBR for humidification of the dry oxygen gas and for the nebulization of antibiotics during anesthesia.[11]

We have used the pentothal-curare apneic technique in conjunction with the PBR in twenty cases. A brief description of this anesthetic technique and some clinical observations follow.

From the Department of Anesthesiology and the Surgical Service of Dr. Arthur S. W. Touroff, The Mount Sinai Hospital.

Received for publication May 23, 1949.

*Now at St. Joseph's Hospital, Far Rockaway, N. Y.

†The device is manufactured by the Mine Safety Appliance Company, Pittsburgh, Pa. It is marketed as the M.S.A. Pneophore and has received acceptance, with reservations, by the Council of Physical Medicine of the American Medical Association.

ANESTHETIC TECHNIQUE

The patient is premedicated with morphine sulfate and atropine sulfate, in varying dosage, one to one and one-half hours before the scheduled operating time. An intravenous drip of Pentothal Sodium (0.4 to 0.6 per cent) is begun in the operating room. The drip is run rapidly until the anesthetized patient's jaw relaxes; *d*-tubocurarine is then injected into

Fig. 1.—The PBR attached to an endotracheal tube with inflated cuff (*A*). The differential pressure valve (*B*) converts continuous positive pressure to intermittent positive pressure. The amount of pressure is controlled by the pressure-regulating valve (*C*).

the tubing of the intravenous drip close to the needle; the average initial dose of *d*-tubocurarine is 15 mg. It is advisable to administer 100 per cent oxygen from an anesthetic apparatus during this period of curarization in order to avoid hypoxia. If necessary, intermittent manual positive pressure is exerted on the anesthetic breathing bag to augment depressed respirations. When the maximum curare effect is observed, usually within three minutes, a cuffed oral endotracheal tube is introduced and attached to the PBR (see Fig. 1). The cuff of the endotracheal tube is inflated until there is no leakage; this is imperative inasmuch as even slight leakage about the endotracheal tube interferes with proper cycling of the differential pressure valve. The pressure-regulating valve is set at 8 to 10 cm. of water, delivering 100 per cent oxygen. If, following intubation, the patient is not in apnea, additional doses of Pentothal Sodium (0.1 to 0.2 Gm.) or *d*-tubocurarine (3 to 6 mg.), or both, are administered until respirations cease. Further doses of Pentothal Sodium and *d*-tubocurarine are given when spontaneous respirations are resumed, provided that a continued state of apnea is desired.

The degree of positive pressure employed during operation is variable. It is important to use the lowest positive pressure compatible with the needs of the patient and surgeon; this can be determined only during the operation. Thus, positive pressure may be increased to inflate the lungs fully, prior to closure of the chest, or the pressure may be decreased, when desired, to facilitate the surgical exposure.

Upon completion of operation, the PBR is disconnected from the endotracheal tube and the latter then attached to an anesthetic apparatus. Controlled respiration (manual) is maintained at a reduced rate in order to elevate the blood CO_2 level, and thus initiate spontaneous respirations. Hypoxia must be avoided. After spontaneous respirations return, usually within five minutes following the cessation of automatic control, the patient is observed until adequate intercostal motion appears. Tracheobronchial aspiration then is performed and the endotracheal tube removed; in thoracic cases, bronchoscopy is done when indicated.

CLINICAL OBSERVATIONS

Our 20 cases included 1 umbilical hernioplasty, 1 thyroidectomy, 1 nephrectomy, 3 cholecystectomies, 2 transthoracic vagotomies, 1 transthoracic gastrectomy, 5 patent ductus ligations, 3 lobectomies, 1 lung decortication, and 2 pneumonectomies. The ages of the patients ranged from 19 to 66 years.

The amount of Pentothal Sodium used in these cases was 0.85 to 1.5 Gm., while that of *d*-tubocurarine was 12 to 36 mg. We observed no fixed time requirement between the various doses of *d*-tubocurarine; in fact, there was considerable variation. Thus, a patient may remain in apnea as long as one and one-fourth hours before additional medication is required; this may be due, in part, to acapnia produced by the PBR which "blows off" into the atmosphere on expiration.

The duration of automatic controlled respiration in our cases ranged from forty-five minutes to three hours. It is of interest to note that, when spontaneous respirations reappear, a form of augmented respiration develops. This apparently is due to the fact that the differential pressure valve will cycle along with the respiratory pattern of the patient.

Except for an initial fall in blood pressure following curarization, no untoward cardiovascular phenomena were observed; this fall in blood pressure was transitory. Oxygenation, as judged by the color of the blood, was good. Hilar manipulation did not initiate coughing or untoward reflex phenomena. Shifting of the mediastinum and paradoxical respiration were absent in the transthoracic

cases. Operating conditions were excellent. It must be emphasized that the work is still in its early phases and that the technique described should be executed only by a skilled anesthesiologist.

SUMMARY

A new technique of automatic controlled respiration is described. The method utilizes pentothal-curare anesthesia and the pneumatic balance resuscitator. A brief clinical report is presented.

REFERENCES

1. Guedel, A. E., and Treweek, Q. N.: Ether Apnoeas, Anesth. & Analg. **13**: 263-264, 1934.
2. Nosworthy, M. D.: Anesthesia in Chest Surgery With Special Reference to Controlled Respiration and Cyclopropane, Proc. Roy. Soc. Med. **34**: 479-506, 1941.
3. Neff, W., Phillips, W., and Gunn, G.: Anesthesia for Pneumonectomy in Man, Anesthesiology **3**: 314-322, 1942.
4. Orton, R. H.: Controlled Respiration, M. J. Australia **2**: 255-259, 1947.
5. Crafoord, C.: Pulmonary Ventilation and Anesthesia in Major Chest Surgery, J. THORACIC SURG. **9**: 237-253, 1940.
6. Mautz, F. R.: A Mechanism for Artificial Pulmonary Ventilation in the Operating Room, J. THORACIC SURG. **10**: 544-550, 1941.
7. Moerch, E. T.: Controlled Respiration by Means of Special Automatic Machines as Used in Sweden and Denmark, Proc. Roy. Soc. Med. **40**: 603-607, 1947.
8. Harroun, P., and Hathaway, H. R.: The Use of Curare in Anesthesia for Thoracic Surgery, Surg., Gynec. & Obst. **82**: 229-231, 1946.
9. Burns, H. I.: Pneumatic Balance Resuscitator, Air Surgeon's Bull. **2**: 306, 1945.
10. Motley, H. L., Cournand, A., Eckman, M., and Richards, D. W., Jr.: Physiological Studies on Man With Pneumatic Balance Resuscitator "Burns Model," J. Aviation Med. **17**: 431, 1946.
11. Motley, H. L., Lang, L. P., and Gordon, B.: Use of Intermittent Positive Pressure Breathing Combined With Nebulization in Pulmonary Disease, Am. J. Med. **5**: 853-856, 1948.